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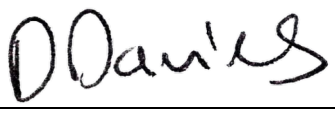	04/10/17

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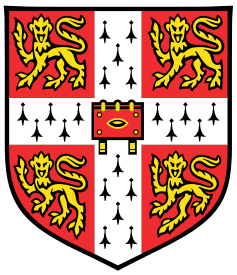

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This dissertation is submitted for the degree of
Doctor of Philosophy

Peterhouse March 2017

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Psychotic experiences beyond psychotic disorders: from measurement to computational mechanisms

Daniel Jay Davies

Abstract

Psychotic experiences (PEs) occur in the general population, beyond psychotic disorders. PEs are a risk factor for mental ill health in young people but can occur benignly in selected samples of adults. Environmental factors predispose to PEs but their underlying mechanisms are not well-understood. Progress in understanding PEs may be limited by diverse conceptualisations, imprecise measurement and a lack of explanatory frameworks that can bridge the gaps between aetiological factors, their effects on the brain and their behavioural manifestations. In this thesis, I undertook a comprehensive investigation of the measurement, health implications, aetiology and computational mechanisms of PEs in adolescents and young adults using data from two large cohort samples, supplemented with smaller-scale behavioural studies.

I first investigated the measurement of PEs. I assessed and optimised the measurement of PEs in young people by two self-report instruments. I then used latent variable modelling to show that a self-report and interview instrument measured the same underlying psychotic phenomena. Both instruments were able to measure severe PEs, while the self-report questionnaire also measured more mild psychotic phenomena.

I then investigated the health implications of PEs. Using cluster analysis in both cohorts, I found replicable patterns of PEs at similar levels of intensity and persistence but with and without depressive symptoms and with varying risk of mental disorder. Paranoid ideation was more associated with depressive symptoms than non-paranoid unusual perceptions and beliefs. Childhood adversity was associated with both PE-prone groups, but later social support from family and friends was far higher in those with PEs and low depressive symptoms than those with PEs and high depressive symptoms.

Subsequently, I investigated the role of the social environment in the development of PEs and psychopathology using longitudinal structural equation modelling. I found that asocial dispositions increased or preceded increase in PEs over one year, mediated by detriment to social support. Conversely, PEs did not precede or increase asociality. I then showed that dimensions of PEs and depressive symptoms were promoted by childhood adversity but differentially affected by later social support, with paranoid ideation being more influenced by support than non-paranoid unusual perceptions/beliefs.

Finally, I investigated specific mechanisms of PEs in two behavioural studies. In the seventh study, I used computational modelling of reward learning to link PEs to reduced ability to modulate learning by confidence, replicating computational effects of a pharmacological model of psychosis. I also used a novel visual task to show that the manifestation of PEs as anomalous perceptions versus anomalous beliefs might be explained by over-reliance on different types of prior knowledge in perceptual inference.

These results suggest that different conceptual approaches to PEs might be synthesised despite issues with their measurement. PEs in young people, while not entirely benign, are heterogeneously associated with psychopathology. Importantly, they characterise a minority of young people who are at very high transdiagnostic risk of mental illness but also occur without distress in young people, often in the context of a supportive social environment. Health outcomes in young people with PEs are predicted and potentially modified by social functioning and social relationships. PEs might arise from atypicalities in how the influences of information sources on perception and belief-updating are modulated according to their reliabilities.

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Introduction

Psychosis is a syndrome featuring abnormalities in thought, perception and emotion that can lead to a loss of contact with reality. Psychotic experiences (PEs) comprise a diverse and complex set of phenomena that are among some of the most bizarre and fascinating studied in clinical neuroscience. PEs are typified by hallucinations, which are percepts occurring in the absence of a stimulus, and delusions, which are fixed, false beliefs that are out of keeping with a person's social or cultural background. PEs characterise psychotic disorders, a set of severe mental illnesses, including schizophrenia, that cause significant morbidity and mortality.

Individual or several PEs can occur without the full syndromes of psychopathology that define psychotic disorders. There is now compelling epidemiological evidence that PEs occur in the general population who do not have any diagnosable mental illness (van Os et al., 2009; Linscott and van Os, 2013; McGrath et al., 2015), particularly in children and adolescents (Kelleher et al., 2012a). PEs occur in 'non-psychotic' mental disorders (Olfson et al., 2002; Hanssen et al., 2003; Yung et al., 2006a; Wigman et al., 2012), both preceding and following the onset of many common mental illnesses (McGrath et al., 2016a). PEs are also associated with diseases not generally considered to be psychotic disorders, like a number of non-psychotic mental illnesses (McGrath et al., 2016a) and Parkinson's disease (Fénelon et al., 2000; Diederich et al., 2009). While the majority of PEs are likely to be transient (Linscott and van Os, 2013) and some have no significant detrimental impact on health (Peters et al., 2016), some PEs may become abnormally persistent or intrusive and mark the onset of a clinical illness like a psychotic disorder (Smeets et al., 2012b; Zammit et al., 2013). Various features of PEs, such as their frequency, their persistence and the amount of distress they cause are thought to contribute to their clinical relevance (van Os et al., 2009). Following the principle that early intervention can improve outcomes in people with psychotic illnesses (McGorry and Yung, 2003), sets of criteria based on the presence of PEs and risk factors have been designed to identify young people at high-risk of psychosis and implemented internationally, though not without challenges (Csillag et al., 2016) and controversy (Pelosi and Birchwood, 2003).

We have limited understanding of the mechanisms by which PEs occur within and outside of psychotic disorders, the aetiological pathways that cause them and the determinants of mental health in people who experience them. There is a pressing need to shed further light on these questions. This is especially important when considering clinical psychosis, in that early psychotic illnesses still tend to go untreated for long periods (Birchwood et al., 2013) and studying subclinical PE may reveal some mechanisms by which clinical psychosis develops. The importance of these questions can also be argued from broader perspectives of psychiatry and public health. High-risk for psychosis criteria also identify young people at risk of nonpsychotic disorders (Kaymaz et al., 2012) and some of those who are at high-risk but who do not transition to a first episode psychosis have fairly poor functional and symptomatic outcomes in the future (Schlosser et al., 2012; Simon et al., 2013). PEs in the general population may be a marker of severe distress (Stochl et al., 2015) and indicate generalised increased risk of mental illness (Kaymaz et al., 2012).

Perhaps the most critical stages of the life course for studying PEs are adolescence and early

adulthood (McGorry, 2011). Most serious mental disorders have their onset around the transition to adulthood (Insel and Fenton, 2005; Kessler et al., 2005) including psychotic disorders (Häfner et al., 1993). This epoch is thought to be critical for development of long-term societal functioning and peer networks (Coleman and Hendry, 1999; Lerner and Steinberg, 2009) as well as aspects of cognition and brain function, particularly related to social relationships (Choudhury et al., 2006; Blakemore, 2012). With respect to schizophrenia, adolescence and early adulthood are considered as a time of both vulnerability to environmental stressors and potential for disease modification (McGorry, 2011; Selemon and Zecevic, 2015), so interventions targeted at this period may be more effective. Given the higher prevalence of PEs than psychotic disorders and evidence that PEs that occur persistently in adults without need for care have their onsets in adolescence (Peters et al., 2016), we can be certain that not all PEs in young people mark the onset of clinical psychosis. PEs in this age range may occur from diverse mechanisms and diverse aetiological influences. Studying PEs in adolescence and young adulthood, particularly in representative samples, should enable us to measure the full distribution of how PEs manifest, capturing phenomena that may indeed be the beginnings of a psychotic illness but also those that may be comorbid with other psychopathology and those that may have no negative health implications, possibly even being beneficial (Mohr and Claridge, 2015).

A significant limitation on our mechanistic understanding of PEs, and indeed of how any mental states arise from physical states, has been the lack of conceptual and methodological frameworks that can bridge levels of explanation, from aetiological factors to neurobiology to cognition, behaviour and subjective experience. The application of methods from computational neuroscience may equip us with the tools to traverse these explanatory gaps (Teufel and Fletcher, 2016). Computational methods focus on using information-processing as an intermediate between physical states and mental states, by mapping out all of the informational quantities and algorithms that could be used to perform a certain function and how they could be physically implemented in a biological system (Marr, 1982). The promise of computational methods have led to the emergence of 'computational psychiatry' (Maia and Frank, 2011; Montague et al., 2012; Corlett and Fletcher, 2014; Wang and Krystal, 2014), a field that aims to apply these methods to the understanding and treatment of mental disorders.

In this thesis, I investigate PEs occurring in adolescents and young adults (hereon referred to as 'young people', for conciseness) in the general population and not limited to psychotic disorders. I do this by drawing on methods from epidemiology, psychometrics and computational psychiatry. In the following review chapters, I describe how I identified a number of important questions that did not have clear answers in the existing literature. In short, I aimed to clarify the dimensionality and measurement of PEs, whether PEs manifest both with and without distress and accompanying mental disorders and what factors determine health outcomes associated with them. This initial set of studies focusing on epidemiological approaches helped me to identify and refine a further set of specific, tractable questions regarding aetiological pathways to PEs and why PEs occur in terms of aberrant information-processing. My experimental approaches to these questions is set out in the latter part of the thesis.

Chapter 1

Review I: Psychotic experiences beyond psychotic disorders in the general population

In this chapter, I will review past and current theories and empirical evidence regarding PEs outside of psychotic disorders, henceforth referred to as PEs for conciseness.

1.1 PEs from the perspective of clinical psychosis: brief historical perspectives

It has long been recognised that psychotic phenomena occur in people without a diagnosable psychotic illness. Isaac Ray, an American 19th century psychiatrist, noted that people displaying subtle psychosis-like manifestations could function well, with the 'insane element... often cropping out in the shape of extravagancies or irregularities of thought or action' (Ray, 1863).

In the early 20th century, psychiatrists including Kraepelin (Kraepelin, 1921), Bleuler (Bleuler, 1911) and Kretschmer (Kretschmer, 1921), described how the onset of psychotic illness was preceded by subtler manifestations of the disease that were also often present in the relatives of patients. At the time, the concept of psychotic illness was undergoing transformation, through Kraepelin's 'dementia praecox' then Bleuler's 'group of schizophenias' (Bleuler and Jung, 1908).

Bleuler advocated a distinction between 'fundamental symptoms' of schizophrenia, caused by the biological disease processes, and 'accessory symptoms' that were brought on by certain 'psychic mechanisms' and included state markers of psychotic episodes, like frank hallucinations, delusions and catatonia. Bleuler's fundamental symptoms included autism (withdrawal from interactions into an internal fantasy world), ambivalence (division of mental states into contradictory tendencies), thought disorder (particularly loosening of mental associations), affective changes and disorders of volition and behaviour. In contrast to Kraepelin, Bleuler considered many of these fundamental symptoms as occurring on a spectrum that was continuous with normality, which may occur in people without needing to be symptoms of mental illness. Bleuler furthered the

argument of continuity with normality by describing 'latent schizophrenias', attenuated forms of the fundamental symptoms that were not necessarily accompanied by accessory symptoms and might not have a deteriorating course. To Bleuler, these were the core of psychosis and were psychosis ('A latent schizophrenia already is a psychosis', Bleuler, 1917).

Kurt Schneider (Schneider, 1925, 1959), influenced by the two approaches to understanding mental phenomena outlined in Jaspers' 'General Psychopathology' (the natural scientific approach investigating the physical or neurobiological causes of disease, and the empathic psychological approach investigating phenomena from the patient's perspective, Jaspers, 1963), emphasised that we must accept the clinical entities of the psychoses as pragmatic constructs. This conservative approach to psychopathology proved influential, helping, along with Kraepelinian traditions, to shape diagnostic systems such as the DSM-III (Association, 1980; Häfner, 2014). Though Schneider considered his classifications atheoretical, this approach formed the skeleton upon which later research attempted to add theoretical and mechanistic flesh, something some argue now limits modern scientific progress (Insel et al., 2010).

Today, the range of 'psychotic disorders' includes schizophrenia, schizoaffective disorder, schizophreniform disorder, delusional disorder, psychotic disorder NOS (not-otherwise-specified), brief psychotic disorder, psychotic depression, psychotic bipolar disorder and substance-induced psychotic disorder. Psychotic disorders have a prevalence of about 3.5%, about 1% of which is schizophrenia.

1.2 PEs occur in the general population, beyond psychotic disorders

There is now a large body of evidence, including individual studies with tens of thousands of participants (McGrath et al., 2015) and meta-analyses (van Os et al., 2009; Linscott and van Os, 2013), that PEs occur outside of psychotic disorders.

A meta-analysis of 62 cohort studies found a median annual incidence of PEs of 2.5% and a prevalence of 7.5% (Linscott and van Os, 2013). These are conservative estimates, given that the analysis included only PEs assessed by interview diagnostic or screening instruments or self-report measurements of specific experiences or phenomena. Around 20% of these experiences were found to be persistent, with the majority being transient and subsiding over time. In an earlier systematic review that used less conservative inclusion criteria regarding PEs, median lifetime prevalence was 5% and median incidence around 3%, again supporting that the majority of PEs are probably transient (van Os et al., 2009).

Different types of PEs probably have different prevalences in the general population. Using cross-national data of PEs in 31,261 adults (McGrath et al., 2015) from the World Health Organisation (WHO) World Mental Health surveys (aged over 18, people with possible psychotic disorder excluded), McGrath et al. reported lifetime prevalence of a narrow set of hallucinatory and delusional phenomena, not attributable to sleep or substance use, of 5.8%, with hallucinatory experiences (5.2% prevalence) being more common than delusions (1.3% prevalence).

Studies reporting prevalence of PEs in children and adolescents tend to report higher preva-

lences than in adult samples. A meta-analysis of 19 population studies found median psychotic experience prevalence of 17% in children aged 9 to 12 and 7.5% in adolescents aged 13 to 18 (Kelleher et al., 2012a). Importantly, this analysis included only interview-verified PEs, or those elicited by a self-report question on auditory hallucinations, shown to have excellent sensitivity, specificity and positive and negative predictive values for psychosis (Kelleher et al., 2011). Use of conservative criteria makes it unlikely that these high prevalences are measurement artefacts. A recent population-based sample of 9,646 adolescents aged 16-19 reported that prevalence of hearing a voice speaking thoughts aloud was 10.6% (Kompus et al., 2015).

Most PEs have their onset in adolescence or young adulthood. A study, again using data from the World Mental Health surveys, showed that the median age of onset of PEs was 26, with the interquartile range from 17-41 (McGrath et al., 2016b). While the age of onset is diverse, these findings, combined with high incidence of PEs, relative to prevalence (van Os et al., 2009; Linscott and van Os, 2013), supports that the majority of PEs occur in this younger age range.

1.3 Theories of psychotic phenomena outside of psychotic disorders

Numerous theories have been developed on why PEs occur. The most influential theories, to date, have centred on the relationship between PEs and clinical psychosis. As a simplification, I will discuss two broad theories and their associated research frameworks that have been used to investigate PEs over recent decades. 'Schizotypy' theories posit that psychotic phenomena are considered the manifestation in personality of the latent liability for schizophrenia. 'Psychosis high-risk' theories posit that some PEs are early manifestations of psychotic disorder, thus indexing high-risk for psychotic illness and potentially facilitating early intervention.

Researchers framing their investigations within one of these perspectives have tended to utilise methodological paradigms from different traditions: schizotypy developing through the lens of individual differences and psychosis high-risk through clinically-orientated research into disease pathology and prediction. These theoretical perspectives are by no means incompatible and have developed alongside one another, often interacting. Indeed, summarising current thinking on PEs is complex due to high volumes of research, heterogeneity of theories and empirical traditions and lack of consensus over organising frameworks, constructs or even terminology. Perhaps the most widely-accepted perspective is to consider PEs as part of a 'psychosis continuum' (Strauss, 1969), though some argue that is has been insufficiently scrutinised and has inadequate empirical support (David, 2010; Lawrie et al., 2010; Lawrie, 2016).

1.3.1 Schizotypy: a distribution of the latent liability for schizophrenia

'Schizotypy' was originally conceived of as the latent liability for schizophrenia manifesting in personality traits. Rado (Rado, 1960) coined the portmanteau 'schizotype' to describe people with a schizophrenia-phenotype; the traits deriving from this phenotype were the 'schizotypal organisation', which manifested as 'schizotypal behaviour'. Rado theorised that a common aetiology could generate diverse clinical and nonclinical outcomes.

Shortly after, Paul Meehl wrote his seminal account of 'schizotaxia, schizotypy and schizophrenia' (Meehl, 1962). In this ambitious work, he described a synaptic atypicality, which he called 'hypokrisia', that occurred across the brain, resulting in a pervasive integrative deficit in the central nervous system that he called 'schizotaxia'. This arose because of a single dominant genetic influence, the 'schizogene', and resulting in a personality organisation, 'schizotypy', that represented 'latent liability' for schizophrenia. Schizotypy was necessary but not sufficient for the development of schizophrenia. If a person could 'compensate' for schizotypy, they might not manifest clinical psychosis. However, 'decompensated' schizotypy was schizophrenia. Thus, Meehl's theory integrated genetic, neurobiological and behavioural levels of explanation to arrive at a mechanistic framework within which we could consider schizophrenia and all manifestations of schizophrenia-like phenomena. Meehl, following Bleuler, actually considered positive PEs 'accessory symptoms' (Meehl, 1990), rather than core features.

Meehl argued schizotaxia had a prevalence of about 10% and represented a discrete taxon, or category, in the population. It was possible, but unlikely, for a schizotaxic person to not develop schizotypy if they developed in a sufficiently benign environment. Meehl's account is sometimes referred to as 'quasi-dimensional', with thresholds or categories underlying a distribution of psychotic phenomena.

1.3.2 Also schizotypy: a fully-dimensional distribution with adaptive and maladaptive manifestation

The schizotypy model was developed further by Gordon Claridge, who proposed the 'fully-dimensional' theory (Claridge, 1997). This posits that schizotypy represents natural variation in the central nervous system that produces variation in behaviour and experience. At its extreme, this confers susceptibility to psychotic disorder, but this variability is fully continuous with normality and can have adaptive or beneficial manifestations too.

Beneficial associations of schizotypy are thought to include creativity, openness to experience and spirituality (Mohr and Claridge, 2015). This emphasis on possible adaptive manifestations has drawn criticism, particularly from researchers like Mark Lenzenweger (Lenzenweger, 2011), a proponent of Meehl's taxonic model, who argue that schizotypy represents ill health, and remains a point of controversy and active investigation.

1.3.3 Schizotypy is multidimensional

Schizotypy, whether considered quasi-dimensional or fully-dimensional, is thought to be multi-dimensional. A large number of studies have attempted to identify the number of dimensions of schizotypy using factor analysis, a method that explains observed data as a function of unobservable, 'latent' variables. The majority of studies support for three or four latent dimensions (Raine et al., 1994; Bergman et al., 1996; Chen et al., 1997; Vollema and Hoijtink, 2000; Reynolds et al., 2000; Fossati et al., 2003; Stefanis et al., 2004; Wuthrich and Bates, 2006; Compton et al., 2009; Badoud et al., 2011; Fonseca-Pedrero et al., 2014; Barron et al., 2015), though with important exceptions (Chmielewski and Watson, 2008).

These dimensions are considered broadly comparable to dimensions of psychotic illness. A 'positive' or 'cognitive-perceptual' dimension (Raine et al., 1994) comprises what I refer to as PEs: distortions of reality, unusual perceptual experiences and anomalous beliefs or ideation, such as paranoia or grandiosity. A 'negative' or 'interpersonal' dimension (Raine et al., 1994) comprises difficulties with social relationships, social anhedonia, lack of close friends, restricted experience and expression of affect and social anxiety. A 'disorganisation' dimension (Raine et al., 1994) comprises unusual or hard to understand speech and eccentric or odd behaviour. Some models include different constructs or separate these constructs further, such as the 'impulsive non-conformity' scale in the O-LIFE questionnaires, devised by Claridge (Mason and Claridge, 2006) or separating a 'paranoia' dimension from the cognitive-perceptual dimension (Stefanis et al., 2004).

1.3.4 PEs as the precursors of psychotic disorders: prodrome and psychosis-risk research

Another critical perspective in the study of PEs outside of diagnosed psychotic disorders is that they can represent the 'prodrome' of psychotic illness. A prodrome is a set of signs and/or symptoms that precede a disease's characteristic manifestations. A prodrome is a retrospective concept; it can only be truly diagnosed once definitive disease markers have developed.

The initial prodrome of psychotic disorders is varied and challenging to identify, but some general patterns have been identified. There is evidence of a progression through unspecific symptoms, followed by 'basic symptoms' (Ebel et al., 1989; Schultze-Lutter and Klosterkötter, 2002; Vollmer-Larsen et al., 2007) (a set of supposedly 'core' symptoms, including subjective disturbances of language, perception, thought and motor function, reduced stress tolerance, altered bodily sensations, changes in emotion, concentration and memory and impaired social functioning (Klosterkötter et al., 2001)), then attenuated forms of PEs, then transient psychotic symptoms, before the onset of a psychotic episode (Schultze-Lutter et al., 2010).

PEs in the general population might therefore represent the early stages of disease. The early promise of prodromal research was that earlier identification and intervention in psychotic disorders would improve patient outcomes and deliver healthcare more efficiently. McGorry & Yung (McGorry and Yung, 2003) clearly laid out the case that interventions for psychotic illness should be as early in the disease course as possible. Contrary to the public perception that interventions for psychosis are ineffectual and psychosis has a poor outcome, there are highly effective treatments that promote symptomatic recovery (Schennach et al., 2012). Delaying access to such interventions, or a greater duration of untreated psychosis (DUP), may confer poorer prognosis in psychotic illness, an observation that dates as far back as Krapelin (Kraepelin, 1921). Recent meta-analyses showed association between DUP and symptom severity, lower probability of remission, poor social functioning and poor global outcomes (Penttilä et al., 2014), as well as poorer treatment response (Perkins et al., 2005) and greater negative symptoms (Boonstra et al., 2012). Intervening early may also allow better management of comorbid psychopathology, which is often present both in psychosis (Buckley et al., 2009) and its prodrome (Rosen et al., 2006).

1.3.5 Synthesis

Researchers in each field have tended to utilise different paradigms. Schizotypy, with its interest in personality traits, has been less associated with longitudinal studies, such as developmental trajectories of schizotypy or long-term health outcomes in people with schizotypal traits (though with important exceptions, like the Chapmans' landmark longitudinal studies (Chapman et al., 1994)). In contrast, the high-risk paradigm, with its interest in prediction of who will and will not develop a psychotic disorder, is fundamentally temporal in nature but tends to consider state symptoms and change over short periods, like worsening psychotic symptoms or decline in functioning. It has focused less on stable, trait-like manifestations of psychotic phenomena.

This is changing, and these fields are perhaps converging (Debbané et al., 2015). Schizotypy has been suggested as an 'organising framework' within which to investigate disturbances to social functioning and affect, as well as psychotic disorders (Cohen et al., 2015). Though the shape of the distribution or what even is distributed in the psychosis continuum is not always made clear, some suggest it is an extension of Claridge's dimensional model and can easily accommodate epidemiological, aetiological and mechanistic work linking psychotic disorders and PEs (Nelson et al., 2013b).

Bringing together methods and theoretical insights from schizotypy and high-risk research could help advance our understanding of psychotic phenomena in both clinical and nonclinical populations. Methods from individual differences research are well placed to investigate heterogeneity and variability. High-risk paradigms tend to be more epidemiologically rigorous, such as in sampling and inference of causality, while schizotypy work has been criticised for commonly using undergraduate samples, cross-sectional studies and self-report measurement.

However, schizotypy, high-risk paradigms and the continuum model all focus on a specific relationship between PEs and psychotic disorders. The reality of the relationships between PEs and psychopathology appears more complex, with significant implications for theoretical and empirical approaches to their study, as I will discuss in the remainder of this chapter.I will discuss how PEs may mark the onset of psychotic disorder but also predict non-psychotic psychopathology and sometimes occur without need for clinical care, supporting that PEs in the general population are associated with diverse health outcomes.

1.4 PEs and related phenomena may mark the early stages of psychotic disorders

1.4.1 Psychotic disorders may arise when nonclinical PEs become aberrantly persistent and cause distress and functional impairment

The majority of PEs are probably transient, supported by their similar prevalence and incidence (van Os et al., 2009) and by longitudinal investigations (Zammit et al., 2013). There is consistent, direct evidence from large-scale longitudinal designs that some psychotic disorders are the result of 'subclinical' PEs becoming persistent and distressing during adolescence and early adulthood

(Chapman et al., 1994; Poulton et al., 2000; Hanssen et al., 2005; Welham et al., 2009; Dominguez et al., 2011; Werbeloff et al., 2012; Zammit et al., 2013).

Poulton et al. (Poulton et al., 2000) showed in the Dunedin birth cohort that 11-year-old children with delusional beliefs or hallucinations had a very high risk of a schizophreniform diagnosis at age 26, with 42% of the cases at age 26 reporting 1 or more symptom at age 11. Importantly, this prediction was specific; it did not predict mania or depression at 26.

In Early Developmental Stages of Psychopathology (EDSP) study, a prospective general-population sample of adolescents (aged 14-17), in which PEs were measured at four times points spanning 8.4 years. Clinical psychosis, defined as PEs with significant functional impairment, had a dose-response relationship with the number of times PEs were expressed at the earlier time points (Dominguez et al., 2011).

A study in the Avon Longitudinal Study of Parents and Children (ALSPAC) investigated the continuity of interview-verified PEs measured at age 12 and age 18 (Zammit et al., 2013). Of the 4060 participants who took part at both time points, 2.5% had PEs (suspected or definite) at both time points, making up 21.3% of the total population with PEs at age 12. 9.1% had them at age 12 only and 4.7% had them at age 18 only. From this, we can infer that 80% of childhood PEs are likely to be subside over the course of adolescence, with 20% persisting. Having PEs at age 12 increased the odds of having PEs at 18, with definite experiences predicting higher odds than suspected ones.

A recent systematic review and meta-analysis examined evidence for prediction of clinical psychosis from nonclinical PEs in the general population (Kaymaz et al., 2012), finding 3.5 times increased yearly risk of conversion to clinical psychosis in people with PEs (0.56% conversion) than those without (0.16% conversion). Importantly, there was, again, evidence of a dose-response relationship with the severity/persistence of PEs.

These studies support that subclinical PEs are mostly transient, but around one fifth of them become persistent. The more PEs persist, the greater the risk of onset of a clinical psychotic disorder.

1.4.2 Operationalised high-risk states can predict development of psychotic disorders and facilitate early intervention but most will not develop clinical psychosis

Different instruments, operationalised criteria and clinical services have been established with the aim of reliably measuring risk of psychotic disorders and identifying individuals with a trajectory towards psychotic illness (Miller et al., 2003; Yung et al., 2005; Riecher-Rössler et al., 2007). The criteria generally require 'attenuated psychotic symptoms' (APS), 'brief limited intermittent psychotic symptoms' (BLIPS) and either familial risk or poor functioning. APS are subthreshold, attenuated positive symptoms, like unusual ideas of reference or paranoid ideation, present for over a week. BLIPS are periods of transient positive psychotic symptoms, occurring for less than a week.

Prospectively identified UHR states are reasonably predictive of conversion to psychotic disorders,

with upper estimates of rate of conversion to psychotic disorders of around 40% (Cannon et al., 2008). A meta-analysis found mean transition risks of 18% at 6-month follow-up, 22% at 1 year, 29% at 2 years and 36% after 3 years (Fusar-Poli et al., 2012).

Thus, while people meeting UHR criteria are at increased risk of psychotic disorders, most people who meet these criteria do not transition. Indeed, it has been observed that rates of conversion to psychosis have declined in more recent studies (Yung et al., 2006b). Most studies, until recently, considered conversion to psychosis and psychotic symptoms as the primary outcome. These studies suggest that around one third of people meeting UHR criteria will transition, while around another third will not convert but remain systematic and functionally impaired, while about a third recovery symptomatically and functionally (Gee and Cannon, 2011). Combining these criteria with other predictors in multivariate analyses, such as basic symptoms, or other symptoms like depression or disorganised symptoms, may improve positive predictive values (Yung et al., 2003; Ruhrmann and Schultze-Lutter, 2010).

The concept of the prodrome of psychosis and psychosis-risk clearly has practical and clinical utility, suggestive of construct validity and continuity between early, clinically relevant PEs and psychotic disorders. However, it is not yet sufficiently clear which PEs are the precursors of psychotic illness and which are not, though differentiation may be possible based on features like persistence and associated distress or functional impairment (van Os et al., 2009). The success of high-risk paradigms lets us conclude that some, but not all PEs in the general population are early manifestations of psychotic disorders.

1.4.3 Schizotypal personality traits in the general population indicate risk of psychotic and non-psychotic disorders, but more evidence is needed

Longitudinal studies of schizotypal personality traits predicting psychotic disorders are uncommon, but generally find that these traits do predict psychosis or personality disorders considered related to psychotic disorders (Kwapil, 1998; Kwapil et al., 2000, 2013; Gooding et al., 2005; Bogren et al., 2010; Miettunen et al., 2011). The specific patterns of association vary according to the outcomes and the measures used.

Studies using the Chapmans' 10-year longitudinal data have produced evidence that 'schizophrenia-spectrum' personality disorders (schizotypal personality disorder, schizoid personality disorder, paranoid personality disorder') are predicted by social anhedonia (Kwapil, 1998) and by both positive and negative schizotypy (Kwapil et al., 2013), while clinical psychosis is predicted by perceptual aberrations and magical ideation (Chapman et al., 1994). This work is limited by hypothesis-driven groupings of deviant scorers as they are likely to be arbitrary definitions and do not capture the full distribution of psychotic phenomena.

To my knowledge, the only study using a representative sample used data from the Northern Finland 1966 Birth cohort (Jääskeläinen et al., 2015), and found that perceptual aberrations concurrently differentiated schizophrenia from other psychotic disorders and psychotic disorders from nonpsychotic psychiatric disorders. Over a subsequent 11-year follow-up period, social anhedonia predicted development of any psychotic disorder, while lower scores on physical anhedonia differentially predicted development of a psychotic disorder versus a nonpsychotic disorder

(Miettunen et al., 2011).

1.4.4 Implications

The link between PEs in the general population and clinical psychosis goes beyond phenomenological similarity. PEs can be early signs of a severe psychotic illness, which explains the drive to understand and utilise them for better clinical prediction and intervention. However, as I will discuss, this link may not be specific, when considering how PEs are related to psychotic and non-psychotic mental illnesses.

1.5 PEs predict nonpsychotic disorders and may indicate general psychopathology

1.5.1 High-risk criteria are associated with risk of nonpsychotic disorders

Recent prospective psychosis high-risk studies have considered a plurality of psychiatric outcomes beyond psychotic disorders and more thoroughly mapped out the health trajectories of people at clinical high-risk for psychosis. In the same meta-analysis that showed PEs in the general population increase risk of psychotic disorders, it was found that they also increase the risk of nonpsychotic psychiatric disorders (Kaymaz et al., 2012), albeit with weaker association. Recent studies have reported a decline in rates of transition to psychosis (Simon et al., 2011; Fusar-Poli et al., 2012). Comorbidity, particularly with depression, anxiety and substance use are common in the high-risk state (de Wit et al., 2014; Lim et al., 2015; McAusland et al., 2015; Azar et al., 2016), suggesting that high-risk criteria may capture people with high levels of generalised psychopathology. In the Chapman's 10-year cohort, positive schizotypy also predicted mood disorders, substance use disorder and any mental health treatment while negative symptoms predicted social impairment (Kwapil et al., 2013).

Non-conversion to psychotic disorder from a high-risk state does not always indicate return to good health and levels of functioning. Meta-analysis of 8 studies (Miller et al., 1999; Haroun et al., 2006; Lemos-Giráldez et al., 2009; Simon and Umbricht, 2010; Addington et al., 2011; Velthorst et al., 2011; Ziermans et al., 2011; Schlosser et al., 2012) that examined remission rates suggests that, while around three quarters of people will not transition to psychosis within two years, only around half of them will achieve remission, suggesting remission rates of up to 35% of the initial high-risk population (Simon et al., 2013). Functional recovery does not always accompany symptomatic recovery (Schlosser et al., 2012) and functioning can still be low, even years after first being identified as high-risk. These results are complicated by using fairly short follow-up periods, as transitions may occur after a longer time (Nelson et al., 2013a), particularly in younger people (Riecher-Rössler et al., 2009; Fusar-Poli et al., 2012).

1.5.2 PEs occur in non-psychotic psychiatric disorders and indicate severity

PEs also occur in people with non-psychotic psychiatric disorders (Olfson et al., 2002; Hanssen et al., 2003; Yung et al., 2006a). In a general population sample of adolescents and young adults (Wigman et al., 2012), around 27% of people with depression or anxiety disorders had at least one lifetime psychotic experience and were 2.2 times more likely to have had a psychotic experience than those without a disorder. Presence of such comorbid PEs in non-psychotic disorder tended to occur in younger participants and predicted poorer illness course. The presence of PEs in non-psychotic disorder is promoted by many of the same risk factors for clinical and nonclinical psychosis (Guloksuz et al., 2015a). Further evidence that PEs occur commonly in other disorders comes from the WHO World Mental Health Surveys, in which McGrath et al (McGrath et al., 2016a) reported that first onset of PEs preceded the onset of 8 of 21 common mental disorders, but that the onset of 18 of 21 disorders were associated with subsequent first onset of PEs.

1.5.3 PEs in the general population indicate severity on a general distress factor that also underlies depressive and anxious symptoms

While there is evidence of some PEs occurring without distress and without need for care, PEs in the general population do commonly occur with subclinical depressive and anxious symptoms (van Nierop et al., 2012, 2014, 2015). As discussed, the onset of PEs precedes development of some common mental disorders (Rössler et al., 2011) and follows development of many disorders (McGrath et al., 2016a). Stochl et al. showed that covariance among PEs and depressive symptoms can be summarised by a latent factor of common mental distress (Stochl et al., 2015), with specific factors explaining residual variance in each domain. Using item response theoretic analyses, the authors showed that PEs uniquely measured a more severe range of the distribution of distress than classical depressive symptoms.

1.5.4 Implications

These sets of findings clearly demonstrate that PEs do not respect current nosological boundaries. Neither does detection of PEs in the general population or at-risk populations necessarily signify specific risk for psychotic disorders. PEs may be a common manifestation of mental distress, similar to general symptoms like low mood, worry, fatigue or sleep disturbance. Such a conceptualisation echoes earlier models of psychopathology as arranged hierarchically (Foulds and Bedford, 1975), in which relatively rarer symptoms, like PEs, are co-expressed with a variety of common symptoms (Sturt, 1981).

This undermines theoretical work that takes clinical psychosis as a landmark and, from there, forms perspectives on nonclinical PEs. While there is clearly phenomenological overlap and association between nonclinical PEs and later psychotic disorders, considering a single continuum that links them is probably an oversimplification (Kaymaz and van Os, 2010).

This has significant implications for public health approaches to mental health (Wahlbeck, 2015), in that it may be important to assess PEs to measure the full distribution of mental distress.

A common distress factor may also partly explain the non-specificity of many environmental (Kounali et al., 2014) and genetic risk factors for mental disorders (Cross-Disorder Group of the Psychiatric Genomics Consortium et al., 2013).

1.6 PEs, even when persistent, are not always associated with clinical illness, distress or impairment

1.6.1 Ultra-high risk states have a low prevalence

Not everyone who has PEs will meet UHR criteria. PEs alone far from qualify a person for high-risk states, though APS are the most common route into UHR status. UHR criteria require a person to be help-seeking, so it is difficult to epidemiologically assess how prevalence UHR states are in the general population. Kelleher et al. investigated prevalence of prodromal syndromes in a sample of 212 adolescents, aged 11-13 and enriched for those scoring highly on a self-report screen for psychotic symptoms (Kelleher et al., 2012c). Using the Structured Interview for Prodromal Symptoms (Miller et al., 2003) criteria, 7.7% met criteria for APS and 3.5% met criteria for BLIPS, with 8.1% meeting UHR criteria overall. Using Comprehensive Assessment for At-Risk Mental States criteria (Yung et al., 2005), 7.7% met criterion for an UHR state, excluding the decline in psychosocial functioning. With the criterion for decline in functioning, just 0.9% of the sample met CAARMS UHR criteria. This suggests that most people with PEs are not impaired by them and not at imminent risk of clinical psychosis.

1.6.2 Some (and possibly most) PEs occur benignly

Evidence that PEs can occur without subjective distress or impaired wellbeing can broadly (and somewhat artificially) be divided into two strands. One strand has considered non-clinical psychotic phenomena in the framework of 'healthy schizotypy', discussed prominently by Gordon Claridge (Mohr and Claridge, 2015). The other strand has investigated discrete PEs occurring without a need for care and auditory verbal hallucinations (AVH), a common type of non-clinical PE, in particular.

Healthy schizotypy is characterised by cognitive-perceptual schizotypy in the absence of interpersonal/negative schizotypy (Mohr and Claridge, 2015). Positive schizotypy has been shown to occur without other schizotypal dimensions and without high levels of distress or impaired wellbeing in a number of studies employing person-centred classification analyses (Loughland and Williams, 1997; Goulding, 2005; Goulding and Ödéhn, 2009; Cella et al., 2013; Tabak et al., 2013; Ruzich et al., 2015; Fonseca-Pedrero et al., 2016). Using a data-driven clustering analysis on positive PEs, disorganisation and negative schizotypy in 420 undergraduates, Tabak et al. (Tabak et al., 2013) found evidence of six distinct clusters of schizotypal trait expression, in some of which the dimensions dissociated. High scores on all dimensions, high scores on negative schizotypy alone and high scores on negative schizotypy and disorganisation predicted poor well-being and quality of life. The presence of positive PEs without the other schizotypal dimensions predicted similar wellbeing and quality of life to people with low scores on all schizotypal traits.

A very similar clustering pattern was recently found by Fonseca-Pedrero et al. in a general population sample of adolescents, with similar associations with mental health (Fonseca-Pedrero et al., 2016). A limitation of this work is it tends to rely on self-report of general trait proneness to PEs, rather than specific PEs or ones that have been validated by an external assessor, like in interviews. Some authors suggest such 'benign' PEs may be artefactual or simply very mild, transient psychotic phenomena (Stanghellini et al., 2012) that are not truly comparable to those occurring in psychosis (David, 2010).

More convincing evidence of non-clinical PEs comes from extensive investigations comparing people with PEs in the context of clinical psychosis and people with PEs but no need for clinical care, that have used interviews or detailed self-report measures to verify psychotic phenomena. Critically, these studies support that non-clinical PEs can occur with a similar intensity and persistence as observed in clinical psychosis (Brett et al., 2014b; Peters et al., 2016). This complicates the idea that persistence of PEs reflects increasing psychopathology or the onset of psychotic disorder. There are replicable differences between clinical and non-clinical PEs. Delusions and odd beliefs tend to be more commonly associated with a need for care (Rössler et al., 2015; Peters et al., 2016). Similarly, PEs that invoke distress (Hill et al., 2012; Johns et al., 2014), PEs occurring in the context of cognitive deficits (Badcock and Hugdahl, 2012) and biases (Daalman et al., 2013) and PEs for which people develop distressing or maladaptive appraisals (Garety and Kuipers, 2001; Peters et al., 2012; Brett et al., 2014a) are more associated with a need for care.

1.6.3 Implications

Not all PEs are associated with distress, impairment or illness, but some of this evidence is complicated by methodological issues related to measurement and sampling. It is not known whether such 'benign' PEs reflect the same underlying mechanisms as clinical PEs but in the absence of additional risk factors or the presence of additional protective factors, or a different underlying mechanism.

1.7 Is continuity between PEs and clinical psychosis supported by overlapping environmental factors involved in the aetiology of nonclinical PEs and psychotic disorders?

There is good evidence from multiple epidemiological studies that some risk factors for psychotic disorders also promote nonclinical PEs, which is often stated as evidence in favour of a psychosis continuum (van Os and Reininghaus, 2016). Nonclinical PEs may share genetic influences with clinical psychosis, given that the earliest observations of PEs outside of psychotic disorders were in the relatives of psychotic patients and PEs, like psychotic disorders, are heritable. Heritability estimates from twin studies range from 15-59% (Ericson et al., 2011; Hur et al., 2012; Zavos et al., 2014).

Factors that predispose to both psychotic disorders and PEs include migrant status or belonging to an ethnic minority (Johns et al., 2002; Cantor-Graae and Selten, 2005; Morgan et al., 2009;

Veling et al., 2010; Linscott and van Os, 2013), cannabis use (Moore et al., 2007; Kuepper et al., 2011b), male sex (van Os et al., 2009), socioeconomic adversity, urbanicity (McGrath et al., 2004; Kuepper et al., 2011a; Vassos et al., 2012), family history of psychotic disorder (Krabbendam et al., 2004; Polanczyk et al., 2010), pregnancy and birth complications (Zammit et al., 2009), developmental impairments (Cannon et al., 2002), low IQ (Cannon et al., 2002; Horwood et al., 2008), distressing life events (Beards et al., 2013), childhood trauma and maltreatment (Varese et al., 2012), victimization by peers (Schreier et al., 2009; Varese et al., 2012), and poor social functioning (Polanczyk et al., 2010).

However, most of these risk factors also predispose generally to most common mental disorders, such as depression and anxiety. Few studies have ever investigated the association between putative aetiological factors and PEs and other disorders within the same studies (Krabbendam et al., 2004; Breetvelt et al., 2010) and only one study has quantitatively tested whether these associations differ across disorders (Kounali et al., 2014), finding that most environmental and familial risk factors predispose equally to depression and PEs. Some specificity was found, in that female sex and a family history of depression predispose more to depression, while abnormal neurodevelopment predisposed more to PEs.

Regarding common genetic influences, a recent study investigated the phenotypic manifestations of genetic risk for schizophrenia by capitalising on results from the Psychiatric Genetics Consortium to calculate polygenic risk scores in an epidemiological cohort of adolescents (Jones et al., 2016). The authors found associations between genetic risk and increased negative symptoms and anxiety disorder, but not PEs or depression. This suggests that the continuum of genetic liability for schizophrenia does not manifest as PEs.

1.7.1 Implications

The paucity of research on this question and the lack of specificity evident in existing research means that the argument that common aetiological factors indicate a specific psychosis continuum is unconvincing. Further research in large samples, possibly stratifying by environmental exposures or genetic factors (van Winkel et al., 2015), may hold more promise to identify specific relationships, should any exist. Given the common overlap in PEs and symptoms of depression and anxiety (Stochl et al., 2015), it is possible that studies will identify few specific risk factors because current nosological boundaries do not reflect underlying mechanisms.

1.8 Discussion

1.8.1 PEs in young people are heterogeneous

The evidence reviewed above supports that PEs in the general population are a heterogeneous set of phenomena with varying clinical relevance. Clearly, some PEs mark the prodrome of a psychotic illness, but these are the minority of cases. Most PEs are likely to be transient and some PEs, even if persisting for years, will never be associated with distress or impairment. PEs feature in a state of high general risk of mental disorders that is associated with high levels of

distress and often with functional impairment. Other features, like social functioning, anhedonia or comorbid depression or anxiety increase the likelihood of developing a psychotic illness from this state.

The success of psychosis high-risk research was reflected in the recent debate over inclusion of 'psychosis risk syndrome' into the Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) as a diagnosable disorder (Corcoran et al., 2010; Drake and Lewis, 2010; Woods et al., 2010; Carpenter and Van Os, 2011; Tandon et al., 2012; Yung et al., 2012; McGorry and van Os, 2013). For the reasons discussed above, as well as concerns over diagnostic reliability, state versus trait nature of the high-risk state and potential for stigma and unnecessary intervention, psychosis-risk was not included as a standalone diagnosis but included as a condition warranting further study, termed the 'attenuated psychosis syndrome' (Tsuang et al., 2013). In this debate, some authors emphasised that high-risk criteria also capture participants at risk of other disorders and that it may be more practical to take a transdiagnostic approach (McGorry and van Os, 2013) that would allow clinical staging of emerging mental illness (McGorry et al., 2014). I argue that the current evidence supports this better than theories of a specific psychosis continuum that considering nonclinical PEs as part of a distribution with normality at one end and schizophrenia at the other. I make three main criticisms of the continuum model of psychosis.

Firstly, what is continuously distributed is sometimes ambiguous or not even stated. Possibilities include a distribution of the latent liability or risk of schizophrenia, a phenomenological continuum of qualitatively similar experiences ranging in intensity, a continuum of distress/impairment associated with PEs and a temporal continuum whereby early, nonclinical PEs can develop over time into clinical psychosis. A significant limitation in disentangling these is that instruments like questionnaires or interviews will probably not be able to fully separate these dimensions, unless designed specifically to do so (Peters et al., 2004; Bell et al., 2006) or to elicit rich phenomenological information (Woods et al., 2015).

Secondly, were we able to prove that psychosis manifests as a continuum from normality to clinical disorder, we would still need to set points on that continuum above and below which we are justified to take certain actions, like interventions (Lawrie et al., 2010). Even if the continuum offered a more parsimonious account of psychosis or mapped better on to aetiology or biology, we would need to know it does better than the existing conceptualisation of categorical syndromes in terms of patient outcomes (David, 2010).

Finally, phenotypic continuity (in whatever dimension) of PEs in clinical and nonclinical populations does not mean that they arise from continuity in underlying mechanisms in terms of information-processing and its neurobiological implementation, or in terms of aetiological factors. I will discuss the challenges of working across such levels of explanation and potential solutions further in the next chapter.

1.8.2 Moving forwards I: recommendations

Below, I outline recommendations to make progress in understanding nonclinical PEs that will shape the investigations in this thesis.

1. PEs require unbiased investigation as transdiagnostic phenomena

Study of PEs in the general population must be disentangled from the study of schizophrenia. The evidence is insufficient for a specific continuum traversing normality, nonclinical PEs and clinical psychosis. In part, this is because the kinds of studies needed to claim specificity have not been done. For example, even studies that have directly compared people with no PEs, with nonclinical PEs and with clinically relevant PEs have almost never included a nonpsychotic psychiatric control group without PEs to show that any effects are PE specific. Studies that could identify specificity, such as in environmental or genetic aetiological factors, support non-specificity (Cross-Disorder Group of the Psychiatric Genomics Consortium et al., 2013; Kounali et al., 2014).

Perhaps more importantly, focusing on the relationship between nonclinical PEs and psychotic disorders, without considering the full range of health outcomes, may limit advances in scientific understanding and clinical practise. Continuing to focus on a specific psychosis continuum could limit progress in understanding the development of mental disorders and changes in experience that commonly occur during childhood, adolescence and early adulthood. Strongly claiming a specific link between nonclinical PEs and schizophrenia is potentially stigmatizing and distressing for a young person who experiences them. Critically, it ignores the plurality of outcomes for a population of non-help-seeking young people with PEs. The most likely outcome appears to be that their PEs will subside without clinical relevance. A small proportion will unfortunately go on to develop clinical psychosis. Another proportion will go on to develop other mental disorders. Another proportion may have persistent mild functional impairment, distress and PEs without ever meeting diagnostic criteria for disorder or seeking help. The reasons that determine outcomes for this population are poorly understood, but we do them a disservice by conceptually and empirically focusing on the minority that will develop a psychotic disorder.

One recently proposed framework may already have gone some way towards generalising and unifying the study of nonclinical PEs as transdiagnostic phenomena: the 'extended psychosis phenotype' (Wigman et al., 2011). Van Os characterises this as the 'behavioural expression of vulnerability for psychotic disorder in populations' (van Os and Linscott, 2012). While this is essentially restating some principles of schizotypy, the formation of a new, mostly-descriptive construct, rooted in epidemiological observations while preserving theoretical features borne out in schizotypy and high-risk research, has the potential to reorganise the field and drive research in fruitful directions. Psychosis as an extended, transdiagnostic phenotype is supported by evidence reviewed in this chapter and may be a sensible generalisation for a field that has been focused narrowly on schizophrenia and psychotic disorders. However, in my opinion, the conceptualisation offered by van Os is still too oriented towards psychotic disorders. PEs in the general population deserve unbiased investigation, considering a plurality of positive and negative mental health outcomes.

2. Strands of evidence might be better integrated if we could integrate different theories of PEs, but any synthesis requires empirical support

It is possible, if not probable, that similar psychotic phenomena are captured by instruments arising from different research traditions, such as schizotypal personality or high-risk states for psychosis. It might be possible to integrate aspects of different theories of PEs into a common framework but synthesis is limited by the tendency to use different instruments to measure PEs and related traits without knowledge of whether they are comparable. Integration might be facilitated by testing whether different instrument types measuring PEs are measuring the same or different things. This would require careful comparison of instruments and, ideally, administration in the same population. If diverse instruments prove to be measuring the same underlying phenomena, we may be able to generalise their findings. It is also important to understand differences in what is being measured. If, for example, interview instruments measuring discrete PEs prove to be measuring more severe psychotic phenomena than a self-report instrument measuring schizotypy, this has significant implications for conclusions drawn from empirical studies.

3. We must look beyond positive PEs to associated traits like distress and social functioning

Our theories should consider the diversity of health outcomes in people with nonclinical PEs and that PEs manifest in conjunction with various other traits. To understand the associated traits and health outcomes associated with PEs, schizotypy presents an excellent foundation upon which to build, having long-considered PEs to be part of a multidimensional construct. Social difficulties feature prominently in schizotypy theories. 'Interpersonal schizotypy', characterised by social anhedonia, lack of close friends, reduced expression of affect, is an important predictor of future health (Miettunen et al., 2011). Social dysfunction is reliably found in high-risk groups (Addington et al., 2008; Velthorst et al., 2010) , with poor (Fusar-Poli et al., 2010; Cornblatt et al., 2012) or declining (Cornblatt et al., 2015) social functioning associated with risk of clinical psychosis. However, it is questionable how specifically this domain is related to psychosis, or how 'schizotypal' it really is; social difficulties are a feature of most, if not all mental disorders. Similarly, 'disorganisation' is considered a dimension of schizotypy, though in some prominent instruments like the Schizotypal Personality Questionnaire (Raine, 1991), this dimension is made up of having odd or difficult to understand speech and having odd habits or perceiving one's self as eccentric. Recent research has emphasised how PEs often manifest alongside common depressive and anxious symptoms (Stochl et al., 2015; Guloksuz et al., 2015b), particularly in those meeting high-risk for psychosis criteria (Woods et al., 2009). We must therefore look beyond positive PEs to broader phenotypic measurements.

4. It is particularly important to investigate PEs in adolescence and early adulthood

As described, many PEs, as well as many mental disorders including psychotic disorders, have their onset in adolescence or early adulthood. Many such PEs will be transient and not survive into adulthood. This developmental epoch spans the full transition from the end of childhood to

adulthood and is a time of significant development of cognition, neurobiology and social relationships (McGorry, 2011). It may represent a time in which environmental influences particularly influence future trajectories of health and functioning, for better or worse. For these reasons, studying PEs in samples of young people that are representative of the general population is critical for improving understanding of PEs and for facilitating treatment or even prevention of psychotic disorders. Working with young people from representative samples is often practically challenging due to issues of ethics and accessibility. This likely explains why the majority of schizotypy work has relied on university samples of undergraduates, who may not manifest the representative distribution of PEs or schizotypal traits. Investigating PEs in adolescence and early adulthood, which I will refer to for conciseness as PEs occurring in 'young people', is critical for understanding their impact on health.

1.8.3 Moving forwards II: key questions

Based on this evidence, I selected three tractable questions to address in the first studies in this thesis.

1. Do existing theories of schizotypy account for dimensionality of PEs and related traits in young people? How well can we measure PEs with self-report instruments?

Theories of schizotypal personality posit that PEs are best considered as a multidimensional set of related traits. While this is well-supported, the exact number and nature of dimensions is not clear. Much has been made of whether schizotypy has e.g. three or four factors, and whether specific features group together. However, some of this work is limited by not investigating the dimensionality at the level of explicitly measured items. Furthermore, many instruments measuring PEs have not been subject to rigorous psychometric analyses to quantify their measurement precision and what range of intensity or severity of phenomena they can measure. These are important properties to know when using these instruments in applied empirical studies.

2. Do instruments designed to measure different theoretical conceptualisations of PEs measure the same underlying phenomena in young people? If so, do they measure the same or distinct severity ranges of PEs?

Instruments measuring PEs but derived through different traditions may measure the same underlying phenomena. This is supported by correlational studies, but not by direct comparison of latent variable models. Different instruments may also measure PEs occurring at different levels of severity and measure them with different levels of precision. This could have important implications for empirical work.

The use of different instrument types, such as questionnaires versus interviews, can dramatically change results, such as estimates of the population prevalence of PEs (van Os et al., 2009), with suggestions that self-report instruments generate many false positives (van Os et al., 2001).

However, 'false-positive' PEs are still associated with increased risk of psychotic disorders (Bak et al., 2003.) and non-psychotic disorders and social dysfunction (van Nierop et al., 2012).

If different PE instruments measured the same phenomena, it would support synthesis of evidence collected using different methods. But if instruments measure PEs (or PEs within a particular severity range) with low measurement precision, empirical work using those instruments would lose power and risk spurious associations. PEs of high and low severity could also be continuous in terms of behavioural phenotype but discontinuous in terms of mechanisms or aetiology. As a further test of convergent validity, I attempted to replicate the findings of Stochl et al. (2015) showing that interview-verified PEs and depressive symptoms measured a common mental distress dimension with PEs measuring the more severe range, using self-report PEs only.

3. Do PEs always co-occur with other symptoms of psychopathology in young people in the general population or can they occur without distress or functional impairment? What factors differentiate between PEs with and without distress?

PEs may be an index of severe distress and a risk factor for mental disorder but can occur without associated psychopathology. PEs occurring without a need for clinical care have been reported in highly selected samples. However, there is not conclusive evidence on whether some PEs occur 'benignly' (i.e. without mental distress and psychiatric risk) in young people in the general population. This suggests that PEs may be heterogeneously associated with risk of mental disorders. Importantly, we do not know the robustness, prevalence and characteristics of any benign PE-prone phenotype in representative samples. Were there strong evidence of a phenotype of benignly-occurring PEs in young people, it would complicate current theoretical models of psychosis risk and clinical strategies of using PEs as the focus of early intervention studies. It is also not known whether PEs occurring with and without distress share computational and aetiological mechanisms. Comparing phenotypes of PEs occurring with and without distress and impairment could reveal risk and protective factors. Some of these factors may be modifiable, such as exposure to childhood adversity or cannabis use, suggesting that it may be possible to intervene to help some at-risk young people learn to live and cope with their PEs, as opposed to trying to prevent or eliminate their PEs.

Understanding PEs in terms of mechanisms requires investigating relationships between different levels of explanation.

Ultimately, to improve our understanding of PEs in the general population we will need to move beyond symptom-based descriptions (Insel et al., 2010). We can consider how behavioural phenotypes, measured using questionnaires and instruments, arise from atypicalities in computations or information-processing, how that information-processing is implemented neurobiologically and how genetic, environmental and gene-environment effects could cause them. I consider these perspectives further in the next chapter, to outline the terms with which I will discuss mechanisms of PEs in the remainder of this thesis.

Chapter 2

Review II: Understanding the mechanisms of PEs in terms of information-processing, its neurobiological implementation and aetiology

The assumption that mental states arise from physical states in the body underpins much modern research in psychiatry and cognitive neuroscience. Biological psychiatry promises that we should be able to identify and correct aberrant mental states by manipulating physical states (Montague et al., 2012). However, there remains a huge explanatory gap in understanding how physical states produce mental states, whether normative or pathological.

Similar explanatory gaps exist between aetiological factors (which we can group into genetics, the environment, and potentially gene-environment interactions) and mental states. We have evidence that some factors make PEs and clinical psychosis more or less likely but cannot explain the full pathways by which those effects occur, even if we know something about its influences on physical states like the pharmacological effects of cannabis or structural brain changes associated with childhood trauma.

Bridging the explanatory gaps between aetiological factors, physical states and mental states might drive progress in psychiatry. Explaining the mechanisms of interventions might let us develop more effective versions or predict in whom they will be successful. Explaining the mechanisms by which an environmental factor predisposes to a disorder might let us develop markers to measure risk and resilience in those exposed. Importantly, explaining the pathways by which aberrant mental states arise from aetiological factors and physical states might reduce the societal stigma of mental illness and provide greater clarity to people who suffer from it and their loved ones.

Bridging these gaps requires more than just advances in technology, such as neuroimaging or genomics. Today, neurobiology can be characterised in unprecedented detail in both humans

and model organisms. However, without some principled way of understanding the function of physical states in the body and how their functions produce mental states, the nervous system will remain a 'black box' with inputs and outputs but little understanding of what goes on inside.

Advances in computational neuroscience offer methods that can help bridge the explanatory gaps. It is now possible to recapitulate behavioural markers of mental states using 'computational' models, in which the informational quantities and the operations performed on them to generate a behaviour are made explicit. Such models are arguably most powerful when expressed mathematically but can be expressed in informal language. Were we to identify neurobiological correlates of those quantities and operations, it would be evidence that those features of the nervous system generate those mental states by performing that information-processing. What computational methods offer is an intermediate level of explanation between the physical and the mental. It could therefore serve as a 'Rosetta stone' (Corlett and Fletcher, 2014), allowing us to translate between physical states and mental states.

The emerging field of 'computational psychiatry' (Maia and Frank, 2011; Montague et al., 2012; Corlett and Fletcher, 2014; Friston et al., 2014; Stephan and Mathys, 2014) attempts to use methods from computational neuroscience to understand aberrant mental states arising in mental disorders. Using computational approaches and mathematical techniques in general should have the advantage of increasing the precision and clarity of theoretical models because theories are mathematically formalised, rather than expressed in purely linguistic terms. In practise, this may not always be the case (Teufel and Fletcher, 2016). Computational approaches to psychiatry are sometimes considered to be opaque and, in their current implementations, unhelpfully mutable and flexible, failing to make sufficiently precise predictions about observations that can be confirmed or refuted.

In this chapter, I will summarise the problem of understanding mental states at different levels of explanation, following the seminal work of David Marr (Marr, 1982) that will shape the discourse in the remainder of this thesis. I will then discuss the promising computational framework of 'predictive processing' (for review, see Clark et al., 2013) that shows promise for understanding normative perception, belief and actions and their atypicalities in mental disorders. I will highlight how this framework can incorporate insights from other fields, particularly reinforcement learning (Maia and Frank, 2011).

2.1 Levels of explanation

Marr outlines three levels of explanation we should consider when trying to understand how physical states give rise to mental states: the 'computational', 'algorithmic' and 'implementational' levels (Marr, 1982) .

The computational level describes what the system is doing and why it is doing it. A full description at the computational level requires defining what a system is doing in terms of informational inputs and outputs. The mapping from inputs to outputs and the constraints placed on the system should be precisely defined. Finally, it should be demonstrated how and why the process is appropriate and adequate to perform the required function.

The algorithmic level describes the representation of specific informational quantities and the algorithms required to perform the function described at the computational level. A full description at this level requires a choice of input and output representations and the algorithms needed to transform one into the other. Marr stresses that there is not necessarily a single mapping across levels of explanation. There are usually a wide range of both representations and algorithms at the algorithmic level that could perform a given computation.

The implementational level describes how algorithmic processing could be physically realised, primarily by a biological system. Again, Marr notes that the same algorithm could be implemented in different ways (Marr, 1982).

Before proceeding, I will define some terms. A representation is 'a formal system for making explicit certain entities or types of information, together with a specification of how the system does this.' (Marr, 1982) Describing something as a formal scheme 'means only that it is a set of symbols with rules for putting them together – no more and no less' (Marr, 1982). Finally, it is important to consider what information a choice of representation captures and what information it loses. Marr write that '[any] particular representation makes certain information explicit at the expense of information that is pushed into the background and may be quite hard to recover' (Marr, 1982).

2.2 Bridging levels: computational psychiatry

Computational psychiatry is an emerging field that aims to apply computational methods and principles to further understanding of mental illness. Computational psychiatry spans two broad approaches (Maia and Frank, 2011; Huys et al., 2016).

The first is applying data-driven analytical methods from computer science and machine learning to psychiatric problems. These methods incorporate and extend traditional statistical analyses. They are well-suited to problems of prediction of outcomes e.g. conversion to psychosis. They are also suited to cluster populations into groups e.g. people with similar symptom profiles.

The second approach is applying theory-driven, 'computational models' that mathematically specify variables and the relationships between them, which may be observed or hidden. These methods give us the tools to specify Marr's algorithmic level, making explicit what we have and have not represented and how performing operations on those representations give rise to computations. Computational models can represent informational quantities and transformations that could plausibly be implemented by the nervous system and used to generate behaviour and experience.

These approaches are complementary and might drive progress on some of the most challenging aspects of psychiatry.

2.2.1 Computational methods may help define mechanistically homogenous disorders

A set of symptoms could be underpinned by different atypicalities in information-processing and neurobiology, meaning disorders with similar symptom profiles may have different underlying mechanisms. A symptom or aberrant mental state, defined at the computational level, could plausibly be caused by more than one mechanism at the algorithmic level. Each form of algorithmic processing might then have multiple possible implementations at the neurobiological level. Marr emphasised this, in saying that levels of explanation could be independent (Marr, 1982). This possible one-to-many mapping from behaviours to mechanisms is a challenge when we attempt to predict or intervene to modify a disease course, as the optimal intervention may be determined by the underlying pathophysiology.

2.2.2 Prediction and targeted intervention based on underlying mechanisms

Having precise information on underlying pathophysiological mechanisms might improve prediction and allow targeted intervention for mental illness. Different interventions would logically be more or less effective based on correspondence between their mechanism of action and pathophysiology. This might enable us to predict and maximise benefit from specific pharmacological medications or psychological therapies.

2.2.3 Principled development of novel interventions

Most of the effective psychopharmacological interventions available in psychiatry have been discovered by serendipity, rather than principled search. A limit on principled development of new interventions is lack of understanding of their underlying mechanisms. Computational approaches may be able to shed light on the pathophysiology of mental illness at a deeper level and so enable precision or individualised medicine in psychiatry.

2.2.4 Integration of biological, psychological and social factors

Computational psychiatry has the potential to comprehensively integrate the biological, psychological and social factors that interact to influence mental health. It could achieve this by translating work at each domain into a common language that makes sense across levels. This is in contrast to biological approaches, which can struggle to describe how subjective experiences arise or how psychological and social factors affect mental health. It is also in contrast to psychological approaches, which might struggle to find plausible and meaningful biological accounts for psychological theories.

2.3 Applying computational principles to perception and belief

I will attempt to describe aberrant percepts and beliefs at the computational, algorithmic and (briefly) implementational levels , by defining how they could arise as deviations from normative

function. I will discuss evidence for this model of how PEs arise and emphasise important questions that I will investigate in this thesis.

By asking broad questions about why PEs arise, we may be able to extract general principles of aberrant experiences and beliefs. However, these questions will, by necessity, ignore some of the complexity of PEs. Understanding specific PEs will require specific computational questions. In this work, I will limit my enquiry to broad questions on the occurrence of aberrant percepts and aberrant beliefs, not in-keeping with the social consensus. This is informed by first considering perception and belief in normative terms (or, at least, how they seem to occur in the majority of people).

2.3.1 Perception at the computational level

I consider perception, at the computational level, as the process of deriving properties of the environment from sensory inputs. This requires going from information detected by sensory receptors into information about what caused it, in a form that facilitates adaptive behaviours and promotes success and survival. The purpose of perception depends on the evolutionary history and environment of the organism in question. An important constraint is that perception involves deriving properties based on current sensory inputs. In other words, perception is the derivation of properties of the environment, spatially-constrained to the immediate environment (which includes internal states of the body) and temporally-constrained to the present moment.

I consider hallucinations and aberrant percepts as inappropriate derivations of properties of the environment from sensory inputs. 'Inappropriate' is fundamentally subjective and refers to deriving properties that are not in keeping with the social consensus. The representations used may be the same as the representations used in perception by the majority but just with different final outputs selected i.e. a normal representation but outputted in the wrong context. The representational outputs in hallucinations may also be fundamentally different and incomprehensible to those of perception in the majority. The 'purpose' of hallucinations is an interesting question; they may be a by-product of evolutionary advantages of heterogeneity in how properties of the environment are derived by members of a social group (Pearlson and Folley, 2008).

2.3.2 Belief at the computational level

I consider beliefs, at the computational level, as knowledge of properties of the environment, including abstract properties for which we have no current or even past sensory data. In these terms, beliefs are stored derivations of properties of the world, not spatially or temporally constrained to the present environment. The process of forming or updating beliefs involves going from information on things in the environment that may be driven by sensory evidence, to information on other statistical regularities, such as relationships between things or features of things. The purpose is probably prediction of spatially and/or temporally distant world states to enable planning, preparing and executing behaviours, including complex behaviours over long periods of time, that promote success and survival.

I consider delusions, at the computational level, as inappropriate stored knowledge of properties of the environment, not constrained to the immediate spatial and temporal context. Like

hallucinations, this is subjective; inappropriate means out of keeping with societal consensus. The representations used may be of things in the world at different levels of abstraction e.g. individual things to relationships between things or temporal changes in things. Delusions, like hallucinations, may be a by-product of evolutionary advantages of heterogeneity in how properties of the environment are derived by social groups (Pearlson and Folley, 2008). From these arguments, it is apparent that beliefs may be computationally very similar to perceptions but not constrained to the immediate spatiotemporal context and stored over time. This may make intuitive sense; it is not unreasonable to think of perception as a belief that something is present in the current environment.

Beliefs could be founded on representations that are separate from sensory inputs, but what would be their value if they had no meaning or implication in the environment or internal states? It is likely that beliefs largely represent relationships between representations empirically defined (at some level) by perception. This can easily be considered as a hierarchy, e.g. moving from sensory inputs to causes of sensory input to relationships between causes of sensory inputs (Mesulam, 1998).

2.4 Aberrant perceptions and beliefs at the algorithmic level

2.4.1 The challenges of inferring properties of the environment from sensations

Recent advances in computational neuroscience make algorithmic models of PEs theoretically and empirically tractable where they were not before (Clark et al., 2013). 'Predictive processing' or 'predictive coding' (Srinivasan et al., 1982; Rao and Ballard, 1999) is currently the dominant computational framework within which to simultaneously consider perception, belief and action (Clark et al., 2013). I will use this framework to discuss mechanisms of normative and aberrant perceptions and beliefs.

At the computational level, I discussed that perception and belief may be deriving the properties of the environment over different spatial and temporal scales. An important constraint is that all the system has access to is information collected by its senses (barring any information that is hard-coded evolutionarily) (Dayan et al., 1995).

Sensory information is not enough to unambiguously derive properties of the environment, for a number of reasons (Helmholtz, 1860). Firstly, it is conveyed by imperfect biological agents (neurons). Secondly, there are potentially infinite mappings from some patterns of sensory information to their causes, such as deriving depth from a 2-dimensional retinal image or deriving whether movement of an image was caused by the eye moving or the environment moving (Helmholtz, 1860). Thirdly, it has no 'teaching signals' (objective information with which to train performance), so the problem is unsupervised. This problem might be aided by correspondence between different sources of sensory information e.g. multisensory integration or by correspondence between personally-derived information and socially-derived information (Boyd et al., 2011). But overall, deriving properties of the environment is limited by separation between organism and environment (Friston, 2013).

The system could solve the problem of deriving environmental properties from sensory information by drawing on past experiences or 'prior knowledge' (MacKay, 1956; Neisser, 1976; Gregory, 1980; Yuille and Kersten, 2006). Current sensory inputs could be compared to stored knowledge of previous inputs and what they were associated with, letting the system derive properties of the current environment by similarity or dissimilarity with previous environments. With the same approach, the system could use stored knowledge from past experiences to predict environmental properties in the future or past (i.e. temporally distant) or for which there is no current sensory data (i.e. spatially distant).

2.4.2 Prior knowledge as a hierarchy of perceptions and belief

Algorithmically, we can think of stored prior knowledge learned from past experiences as internal models of statistical regularities between observed patterns of sensory evidence and their 'hidden' causes (Lee and Mumford, 2003; Friston, 2005, 2010). 'Hidden' denotes that they are not directly observable. Causes can vary over scale and nature. For example, in the visual system, a cause could be an edge, a shape, an object or a scene. Importantly, tracking statistical regularities would let the system define internal models empirically without any teaching signals.

Regularities between causes can themselves be tracked by other internal models, effectively layered on top of one another: these edges make this shape, which is the shape of this object, which is usually present in this scene. This can be considered as a hierarchy of processing levels (Mumford, 1992). At lower levels, internal models are more closely concerned with current sensory inputs. In other words, lower levels derive properties of spatially and temporally constrained sensory information i.e. perception. At higher levels, these internal models become increasingly abstracted from sensory input (Mumford, 1992; Mesulam, 1998). In other words, higher level internal models track regularities between things that may not be spatially and temporally constrained by sensory input, so might plausibly be considered 'beliefs'.

2.4.3 Predictive processing: from internal models to abductive inference

To compare current inputs to stored knowledge, internal models can generate predictions of what sensations would arise from a given hidden cause. These predictions can be likened to hypotheses that can be tested against observed sensory data (Gregory, 1980). By calculating an index of how well predictions match sensory data and comparing a family of predictions from different models, the system can infer the most probable cause of its inputs and thus the most probable properties of the environment. This is an abductive inference (Peirce, 1974); internal models describe how causes result in sensory evidence, while predictive processing enables the system to go in the opposite direction, from sensory evidence to causes. In these terms, we consider sensory evidence entering the hierarchy at the lowest level and being fed forward from low levels to higher levels. 'Feedforward' is sometimes used synonymously with 'bottom-up' or 'ascending'. We consider predictions as being 'feedback' or 'top-down', coming from higher hierarchical levels to lower levels. Inference over the causes of low-level sensory information, constrained to the current spatiotemporal context, would correspond to perception. Inference over causes at higher hierarchical levels, not constrained to sensations in the current spatiotemporal context, might

correspond to inference of more abstract properties.

In algorithmic terms, the system could therefore derive properties of the environment using information on current sensory inputs, predictions from stored knowledge and a way of comparing the fit of predictions to inputs to select the best-fitting one. In other words, the system must calculate the probability of different hypotheses being true, given observed evidence (their 'posterior probabilities'), and then select between them. The comparison of fit of predictions to inputs could be performed by calculating 'prediction errors', analogous to residuals in a regression analysis. The best-fitting hypothesis would be the one that generates fewest prediction errors (i.e. maximises predictive accuracy).

This framework can be extended to accommodate action by essentially equipping it with reflex arcs and allowing it to minimise prediction errors not by updating internal models but by changing the locations of its sensory detectors to match predictions, a process termed 'active inference' (Friston, 2003; Friston et al., 2010; Brown et al., 2011).

2.4.4 Learning by updating internal models using prediction errors

Within this scheme, prediction errors can reflect failure of internal models to predict sensory inputs, suggesting the models may be suboptimal e.g. the environment has changed. Prediction errors can drive updating of internal models and the predictions they generate to accommodate new information. Predictions from an updated model may better explain sensory input, so minimising or 'explaining away' prediction errors. The updated model therefore better captures the causes of sensory inputs. Within this scheme, updating internal models at higher hierarchical levels reflects learning and updating of beliefs. In other words, sensory information enters the system, is transformed at every stage into only its unexplained component (prediction error) and reverberates through the system, changing predictions, until the set of predictions that minimise prediction error across all levels is identified. What the system is doing is therefore maximising prediction of its incoming information.

2.4.5 Modulating learning by the reliability of prediction errors and prior knowledge

Predictions may fail to explain sensory evidence, generating prediction errors, because of noise rather than because the models generating those predictions are suboptimal. The greater the noise in the prediction error signal, the less useful they are and the less they should shape inference and model updating. When sensory information is rendered variable by noise, such as visual information in poor illumination, it could be inefficient to minimise that error to derive properties of the environment. Similarly, when predictions from internal models are known to be highly reliable in the current context, it would not make sense to be over-ready to update those internal models based on isolated instances of prediction error.

Both the variability in prediction error and in predictions can be described by their 'reliability' or 'precision', which is the inverse of variability. The more precise a prediction error, the more likely it is that it reflects meaningful information and predictions should be updated to minimise it. The more precise a prediction is, the more likely it is that it already captures true statistical

regularities and its predictions should not be changed. The relative precision of different information sources (predictions and sensory evidence/prediction errors) thus shapes their influence on model updating and learning (Knill and Pouget, 2004).

The optimal way to combine probabilistic information sources is defined by Bayes theorem (Bayes and Price, 1763). Weighting each information source by its precision accommodates changes in the quality of information sources in different circumstances (Knill and Pouget, 2004), like varying illumination. Precision could also be important when considering actions or updating models with significant consequences e.g. inferring that a trusted friend has intentionally harmed you would need very good evidence, otherwise it is more likely that harm was unintentional.

2.4.6 Aberrant perceptions and beliefs at the algorithmic level

To recap the computational level, I considered aberrant perceptions as false inference of properties of the current spatiotemporal environment and aberrant beliefs as prior knowledge that misrepresents statistical regularities in the environment, not limited to the current spatiotemporal context. Both could arise from deviation of functioning of the algorithmic predictive processing scheme outlined above. Specifically, they could arise from perturbations to the precision or precision-weighting of information sources (Corlett et al., 2009; Fletcher and Frith, 2009).

Aberrant perceptions could arise from over-estimating the precision of predictions (equivalent to underestimating the precision of sensory prediction errors), such that they have an overly-strong influence on inference of environmental properties. This might let something be inferred as the cause of sensations despite poor evidence (Behrendt, 1998; Aleman et al., 2003), manifesting as a false or inappropriate percept.

Atypical internal models might be arrived at through inappropriate model updating from prediction errors that are not tied to meaningful statistical regularities or changes in regularities in the environment. Specifically, this could be caused by weighting the precision of prediction errors as relatively higher than top-down predictions (Fletcher and Frith, 2009; Corlett et al., 2010; Adams et al., 2013). This is fully consistent with 'aberrant salience' accounts of delusion formation that posit inappropriate formation of associations (Kapur, 2003).

These theories can seem opposing (Corlett et al., 2016): one posits that the system ignores prediction errors while the other posits that it learns too much from prediction errors. One resolution to the apparent paradox is to suggest that the former explanation explains hallucinations while the latter explains delusions. But this would be inconsistent with evidence that aberrant percepts and aberrant beliefs co-occur more commonly than they occur independently so proffering two distinct explanations for the two phenomena is unsatisfying in its lack of parsimony. A possible reconciliation may be arrived at by considering the hierarchical nature of information processing. Both over-influential and under-influential prediction errors might co-occur at different levels of a processing hierarchy.

False derivation of causes of current sensory inputs (spatially and temporally constrained) could be driven by ignoring prediction errors at low sensory levels (equivalent to excessive influence of predictions at low levels). Aberrant internal models could be arrived at because of excessive influence of prediction errors at higher levels. These could co-occur for a number of reasons.

Firstly, over-influential predictions may generate over-influential prediction errors at high levels. Secondly, aberrant prediction errors at low levels may be suppressed by over-reliance on predictions, but there may be a limit to this suppression. If aberrant prediction errors 'break through' at this level, they may be represented as highly precise and drive updating of aberrant relationships between things in the environment. Finally, aberrant inferences themselves may cause prediction errors elsewhere by violating predictions from other models, particularly higher-level models that track regularities between things .

2.5 Evidence supporting disrupted predictive processing as a mechanism of PEs

Multiple lines of evidence support disrupted predictive processing associated with PEs. Not all this work has been carried out in both clinical psychosis and in populations with nonclinical PEs.

2.5.1 Impaired low-level sensory processing could cause unreliability of sensory evidence

One line of evidence that supports disruption to predictive processing is evidence of abnormalities in sensory processing associated with psychosis. Disruptions to the precision (i.e. reliability) of sensory information, or to the estimation and signalling of precision of sensory information, could cause changes in updating and use of internal models (outlined above) that distort experience of reality. The outputs of early stages of sensory processing may come to be poor representations of the environment and inputs to complex, higher-level computations that shape behaviour and subjective experience might become less well-structured and less reliable.

Psychosis-associated changes in visual and auditory processing have been best studied, compared to other sensory modalities. The literature on perceptual processing in schizophrenia is rich and complex; a full review is beyond the scope of this thesis.

2.5.2 Approaches to early sensory processing: gain control and integration

Butler, Silverstein and Dakin (2008) grouped early visual deficits into impairments of 'gain control' and 'integration' (Butler et al., 2008). Comparable processes exist in the auditory system (Robinson and McAlpine, 2009) and may provide a useful framework to think about the computations carried out in the early sensory processing stages. Gain control refers to processes that optimise information-signalling with respect to the surrounding context. (Butler et al., 2008). Gain control computations can be considered as increasing the precision of low-level sensory information by improving the integrity of how the system registers sensory events. Integration refers to processes that link lower-level stimuli into more complex stimuli, such as linking local features into global stimulus properties (Butler et al., 2008). Integration therefore refers to a diverse set of computations, including those that might be termed 'perceptual organisation'.

2.5.3 Abnormalities in gain control processes associated with PEs

Deficits in visual gain control associated with clinical psychosis are evident in contrast sensitivity (Slaghuis, 1998; Kéri et al., 2002) and in abnormal effects of surrounding context ('surround suppression') on perception of contrast (Robol et al., 2013; Schallmo et al., 2013, 2015; Tibber et al., 2013; Yang et al., 2013; Serrano-Pedraza et al., 2014), supported by reduced contextual effects on BOLD signal (Seymour et al., 2013). Abnormal visual surround effects are not likely to be global but rather specific for certain types of information, such as contrast or size, rather than luminance or orientation (Tibber et al., 2013), which may reflect deficits at later stages of early visual processing. In the auditory domain, aberrant gain control may be suggested by schizophrenia-associated deficits match tones after a delay (Strous et al., 1995; March et al., 1999; Gold et al., 2012b), but normal influences on performance of distracting stimuli (Rabinowicz et al., 2000) and delay (Javitt et al., 1997), suggesting problems accurately encoding tone information. This could be due to failure to adequately modulate the gain on auditory sensory detectors.

There is less evidence on gain control deficits associated with nonclinical PEs or psychosis high-risk states. Studies have reported increased visual surround effects of contrast (Kéri and Benedek, 2007), and reduced surround effects of size (Uhlhaas et al., 2004), though the size effect may be explained by reaction time (Bressan and Kramer, 2013).

Abnormal gain control in psychosis is possibly supported by reduced evoked brain responses to visual stimuli (Butler et al., 2005, 2007; Martínez et al., 2015) and by reduced 'mismatch negativity' (MMN) (Urban et al., 2008; Csukly et al., 2013; Neuhaus et al., 2013; Farkas et al., 2015), an electrophysiological response to deviant or oddball stimuli that may be a marker of prediction error and its influence on internal models (Garrido et al., 2009). Reductions in the auditory MMN in schizophrenia are reliable and of a large effect size (Umbricht and Krljes, 2005). Reductions in auditory MMN are also evident in psychosis high-risk groups (Brockhaus-Dumke et al., 2005; Atkinson et al., 2012), with some evidence of larger MMN reductions in those who later converted to clinical psychosis (Bodatsch et al., 2011; Shaikh et al., 2012). There is mixed evidence of MMN reductions in first-degree relatives of people with schizophrenia, with evidence of reductions and no reductions (Bramon et al., 2004; Magno et al., 2008). Both reduced (Murphy et al., 2013) and increased (Bruggemann et al., 2013) auditory MMN have been found in young adolescents with PEs, compared to those without PEs. In adults, a larger MMN correlated with paranoid ideation, measured by the Suspiciousness scale of the Schizotypal Personality Questionnaire (Broyd et al., 2016). To my knowledge, no studies have examined the visual MMN associated with PEs outside of psychotic disorders.

2.5.4 Abnormalities in integration processes associated with PEs

Clinical psychosis is also associated with deficits in various processes thought to depend on integration computations (Uhlhaas and Silverstein, 2005; Silverstein and Keane, 2011), including contour integration (Schenkel et al., 2005; Silverstein et al., 2006, 2009; Kurylo et al., 2007; Sehatpour et al., 2010), perceptual grouping by similarity (Uhlhaas et al., 2006; Kurylo et al., 2007), recognition of fragmented drawings (Sehatpour et al., 2010) and integration of moving

stimuli (Cocchi et al., 2007; Tschacher et al., 2008). Phenomenologically, deficits in integration would fit with descriptions of altered experience in psychosis, such as only seeing parts of on object or fragmentation of the visual field, rather than forming holistic percepts (McGhie and Chapman, 1961). In the auditory domain, schizophrenia is associated with deficits segregating auditory streams (Ramage et al., 2012; Weintraub et al., 2012) and abnormal electrophysiological markers of auditory pattern perception (Coffman et al., 2016; Haigh et al., 2016).

As with gain control, there is less evidence regarding atypicalities in integration associated with nonclinical PEs, schizotypal personality traits and people at high-risk of psychosis. In studies investigating processing of global percepts, rather than local details, schizotypy has been associated with both disadvantage (Goodarzi et al., 2000) and advantage (Granholm et al., 2002). A recent meta-analysis showed deficits in Gestalt figure perception when groups at high-risk for psychosis were compared to controls (Panton et al., 2016). However, there was no evidence of deficit when healthy participants with high schizotypy-scores were compared with controls or evidence of correlation between deficits and schizotypal traits (Panton et al., 2016). To my knowledge, early auditory perceptual organisation has not been directly investigated in PEs outside of clinical psychosis.

While aberrant gain control and integration processes are robustly associated with clinical psychosis, inconsistent results in those with PEs or in groups at high-risk for psychosis necessitates further investigation.

2.5.5 Effects of abnormalities in early sensory processing on higher functions

The impact of impairments in gain control and integration on higher functions, like perceptual inference, memory or attentional allocation, may be diverse. A growing number of studies have examined these relationships directly, linking gain control deficits to deficits in encoding stimuli into visual working memory (Dias et al., 2011), reading (Martínez et al., 2013) and object recognition (Calderone et al., 2013). Deficits in tone perception contribute to social difficulties in schizophrenia, in that inference of emotions (Gold et al., 2012b; Kantrowitz et al., 2013) and attitudes (Kantrowitz et al., 2014) from prosody is impaired.

The effects on higher functions could depend on how the system adapts to this unreliability. If the unreliability in inputs is properly signalled and the relative precision of incoming sensory information is down-weighted, the system may come to rely more on other sources of information or from predictions from higher-level internal models for functions like perceptual inference. This is consistent with suggestions of overly-strong influences of expectations or predictions on perception in psychosis (Behrendt, 1998; Aleman et al., 2003; Corlett et al., 2009). Overestimating the precision of incoming sensory information (which may in fact reflect failing to down-weight it) could lead to inappropriate updating of internal models. This is consistent with evidence of sensory information being overly influential in psychosis in various paradigms, such as smooth pursuit eye movements (Hong et al., 2005, 2008; O'Driscoll and Callahan, 2008) or matching of somatosensory forces (Shergill et al., 2005). These atypicalities can be framed as predictive deficits, particularly in corollary discharge mechanisms that down-weight the sensory consequences of self-generated actions (Blakemore et al., 2000; Farrer et al., 2004; Lindner et al.,

2005), and plausibly explain certain phenomena like delusions of control or other experiences of abnormal agency. Similar deficits in 'self-monitoring' have been shown in relatives of patients with schizophrenia (Hommes et al., 2012), in people at high-risk for psychosis (Johns et al., 2010) and with nonclinical PEs (Teufel et al., 2010; Oestreich et al., 2015; Roché et al., 2015).

These lines of evidence suggesting both excessive and deficient influence of predictions on information-processing can seem opposing. More recent work has begun to investigate whether both can be accommodated by appealing to the hierarchical nature of information-processing, considering interactions or compensations across processing stages.

Schmack et al. (2013) investigated the interaction of low-level sensory processing and higher-order beliefs in a large sample of healthy volunteers. Delusional ideation was associated with reduced stability of a bistable stereoscopic illusion of a rotating sphere that could be perceived rotating in either direction. Participants were then given a pair of glasses they were told would bias the direction of rotation. In fact, the glasses did nothing but participants went through a training phase in which the direction of rotation was biased to be one direction over the other, to generate a belief that the glasses would change perception. In a final test phase, the fully bistable illusion was presented again while participants wore the glasses to measure the influence of the learned belief on perception. Delusional ideation, and the conviction people felt in their delusion-like beliefs, predicted stronger influence of the glasses-belief on the perceived rotation of the sphere, which was reflected in connectivity between prefrontal regions and early visual cortices measured using fMRI (Schmack et al., 2013).

Similarly, Teufel et al. (2015) investigated the influence of experimentally-acquired prior knowledge on perception of natural images, binarised into black and white 'two-tone' images so as to appear meaningless. However, after viewing the natural images from which the two-tone images were made, participants were able to clearly see the two-tone image content, such as embedded figures of people or animals. In a task that measured objective ability to discriminate the content of two-tone images, people at high clinical risk for psychosis (ARMS), compared to healthy controls, showed similar initial discrimination of two-tones but greater improvement in discrimination after viewing the natural images, suggesting a stronger influence of higher-order predictions from prior knowledge on perception. In a sample of healthy volunteers, proneness to anomalous perceptions correlated with improvement in discrimination from viewing the natural images, supporting that this may be a common mechanism of clinical and nonclinical PEs.

2.5.6 Resistance to visual illusions

A number of recent articles have emphasised the value of visual illusion paradigms to develop our understanding of psychosis (Notredame et al., 2014; King et al., 2016). Illusions are often described as measuring 'top-down' influences on vision, and the resistance to some illusions seen in schizophrenia taken as evidence of reduced influence of top-down processing (Notredame et al., 2014). This approach has been criticised (Barlow, 1997). There is a significant risk of over-simplification in suggesting illusions have common mechanisms. Illusions probably arise from diverse mechanisms, as was recently suggested by low correlation between individual differences in surround suppression effects of contrast and motion in healthy volunteers (Yazdani et al., 2015). Some of these illusions, such as size illusions or contrast illusions, may better be considered as gain

control effects and may not be mediated by top-down effects. Nonetheless, evidence of reduced susceptibility to illusions in psychosis supports altered integration of information sources when generating percepts. In depth-inversion illusions, concave objects are falsely perceived as convex, such as faces in the 'hollow mask' illusion. Patients with schizophrenia are less susceptible to this illusion (Schneider et al., 2002; Koethe et al., 2006; Dima et al., 2009), with illusion resistance normalising in psychosis patients after admission and treatment on an inpatient unit (Keane et al., 2013). Importantly, resistance to depth-inversion illusions is evident in people at high-risk for psychosis and people in early stages of psychotic illness (Koethe et al., 2009), suggesting it may be a key mechanism of all forms of psychotic experience, rather than being associated only with illness severity, chronicity or intervention.

2.5.7 Atypical reinforcement learning and aberrant salience

Studies of reinforcement learning measure processes of prediction error-driven learning. When complemented with computational modelling of behaviour, such studies present a powerful tool to investigate atypical information-processing associated with PEs.

Schizophrenia is associated with deficits in behavioural tasks measuring learning of reward contingencies through experience ('reward learning') and in rapid changing of strategies when environmental contingencies change ('reversal learning'). Studies using computational models in chronic schizophrenia patients support that the disease and negative symptoms, in particular, are associated with impaired learning from rewards, with often spared learning from punishments, consistent with a rigid and inflexible learning style and failure to learn adaptively from prediction error (Gold et al., 2008, 2012a; Murray et al., 2008b; Koch et al., 2010; Gradin et al., 2011; Strauss et al., 2011; Waltz et al., 2011). Due to the heterogeneity and often widespread impairment in schizophrenia patients, some of these findings may be partly explained by deficits in working memory (Collins et al., 2014; Culbreth et al., 2016), which are considered a key feature of the disease (Goldman-Rakic, 1994; Lee and Park, 2005).

Fewer studies have examined prediction error-driven learning in early psychosis and nonclinical PEs. Reward and reversal learning were shown to be aberrant in a large sample of unmedicated first episode psychosis patients, particularly associated with negative symptoms (Murray et al., 2008a), consistent with results in chronic disease.

Some studies suggest different computational changes across nonclinical PEs or early clinical psychosis and chronic psychotic disorders. Using a task that measured adaptive and aberrant salience mechanisms using the speed of reaction times for decisions in the presence of relevant and irrelevant conditioned stimuli, Roiser et al. found that medicated patients did not display aberrant salience, but instead displayed reduced adaptive salience, compared to controls (Roiser et al., 2009). Using the same task, schizophrenia patients with treatment-resistant persistent delusions were also found to have reduced adaptive salience but not aberrant salience (Abboud et al., 2016). When the same task was used with people meeting ultra-high-risk criteria for psychosis, they displayed normal adaptive salience but increased aberrant salience, compared to controls (Roiser et al., 2013). Similarly, another study showed some evidence that people with subclinical delusional ideation display implicit aberrant salience at intermediate levels, between health controls and schizophrenia patients (Pankow et al., 2016). This raises the possibility that different

stages of psychotic illness might be associated with different computational changes.

2.5.8 Aberrant perceptions and beliefs at the implementational level

A full discussion of how atypical processing at the algorithmic level might be implemented neurobiologically is beyond the scope of this work. To keep this review focused, I have included a limited discussion in Appendix A.

2.6 Discussion

The application of computational methods and principles to psychiatry holds a number of promises (Teufel and Fletcher, 2016). It could enforce precision by demanding that theories can be expressed in formal terms (i.e. mathematically). It could enable translation of existing work in psychology and neurobiology into a common language and facilitate integration and collaboration. It could also bridge the explanatory gaps between mental states, neurobiology and aetiological factors, furthering our understanding of how people develop and recover from mental illness as departure from and return to adaptive/normative functioning. The application of data-driven analyses also has much to offer for classification and prediction, which may lead to improvements in understanding disease heterogeneity and comorbidity and in early intervention or prevention of mental illness.

The success of computational approaches is reflected in the popularity of predictive processing frameworks. These posit that the brain performs statistical inference about the environment and its internal states by building generative models of statistical regularities. Predictive processing offers novel ways to conceptualise psychotic phenomena and to integrate different theories within a computational scheme that could plausibly be implemented by neuronal circuits. Disruptions to predictive processing is far from a full explanation of why PEs occur. Rather, it presents a framework within which to construct and test models to explain changes in mental or physical states in psychosis.

In the remainder of this thesis, I interpreted evidence regarding the manifestation, aetiology and health implications of PEs in the general population in the computational terms of the predictive processing framework, drawing on Marr's principles of levels of analysis to attempt to provide clear and testable theories that can bridge levels of explanation. Based on the principle of integrating data-driven and theory-driven work, I set out first to answer the three key questions described at the end of the last chapter, then to review those findings and decide on tractable theory-driven studies that would shed further light on the aetiology or mechanisms of PEs.

The questions were:

- Do existing theories of schizotypy account for dimensionality of PEs and related traits in young people? How well can we measure PEs with self-report instruments?
- Do instruments designed to measure different theoretical conceptualisations of PEs measure the same underlying phenomena in young people? If so, do they measure the same or distinct severity ranges of PEs?

- Do PEs always co-occur with other symptoms of psychopathology in young people in the general population or can they occur without distress or functional impairment? What factors differentiate between PEs with and without distress?

Chapter 3

Methodology

3.1 Data-driven research questions

At the end of Chapter 2, I discussed the following three questions:

3.1.1 Do existing theories of schizotypy account for dimensionality of PEs and related traits in young people? How well can we measure PEs with self-report instruments?

Latent dimensionality can be investigated using factor analytical methods on responses on questionnaire items in a sufficiently large sample. These methods can be used to test models of dimensional structures based on the literature. Should those models prove insufficient, these methods can be used in an exploratory data subset to identify novel structures and compare how well novel and literature-derived models perform when tested in a non-overlapping validation subset. Measurement precision can be quantified using methods from factor analysis and item response theory.

3.1.2 Do instruments designed to measure different theoretical conceptualisations of PEs measure the same underlying phenomena in young people? If so, do they measure the same or distinct severity ranges of PEs?

Factor analytical methods to investigate latent dimensionality could shed light on these questions, given sufficient sample size and measurements. Importantly, the fit of different latent model structures to data can be compared, such as a unidimensional model, correlated factors models and bifactor models (with a general factor explaining some variance in all items and specific factors explaining variance in some items). Again, measurement precision can be quantified using methods from factor analysis and item response theory. In particular, it is possible to map out over which parts of a distribution a given item is able to discriminate participants. Considering a distribution of increasingly severe psychotic phenomena, this mapping would reveal the severity range of PEs measured by items and instruments. I also followed the analysis pathway of Stochl et

al. (2014) to test whether I could replicate their findings of a common distress factor underlying PEs and depressive symptoms using self-report instruments only.

3.1.3 Do PEs always co-occur with other symptoms of psychopathology in young people in the general population or can they occur without distress or functional impairment? What factors differentiate between PEs with and without distress?

Cluster analysis aims to separate the population into homogenous subgroups. Combined with approaches from machine learning and psychometrics to assess the optimal number of clusters and their robustness, these methods could test whether PEs occurring without distress form a reliable phenotype and how prevalent that phenotype is. Comparison of phenotypes without distress or PEs, with PEs but no distress, and with distress and PEs, could reveal risk and protective factors for distress and impairment in people prone to psychotic phenomena. Comparing these phenotypes on factor scores estimated from latent variable modelling of combined PEs and distress could help resolve why PEs are an index of extreme distress while occurring benignly in some people.

3.2 Data sources

These planned studies require large datasets with measurements of PEs, depressive symptoms, mental disorder and putative aetiological factors. Preferably, these datasets would be collected using principles of epidemiological sampling to ensure the samples are representative of the wider population.

Two datasets collected by researchers at the University of Cambridge are suitable for this set of analyses: the ROOTS cohort and the Neuroscience in Psychiatry Network (NSPN) cohort. Both cohorts utilised a wide range of instruments. I highlight the most relevant instruments for the investigating the questions outlined above.

3.2.1 ROOTS

ROOTS is a longitudinal study of adolescence (Goodyer et al., 2010; Lewis et al., 2016). The study aimed to identify the biological bases of mental illnesses and their sub-clinical manifestations in young people. The study investigated the roles of genetic, environmental, social and psychological factors in pathways to mental illness. ROOTS was funded by the Wellcome Trust. Ethical approval for the ROOTS study was granted by Cambridgeshire 2 REC, in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. At study entry, all participants and their parents gave written informed consent. The ROOTS sample was largely representative of Cambridgeshire in terms of socioeconomic status.

The study involved assessments at three time points (T1-3): T1 at age 14, T2 at age 15.5 and T3 at age 17. A summary of the recruitment, time points and relevant assessments is shown

Figure 3.1:Cohort diagram: ROOTS

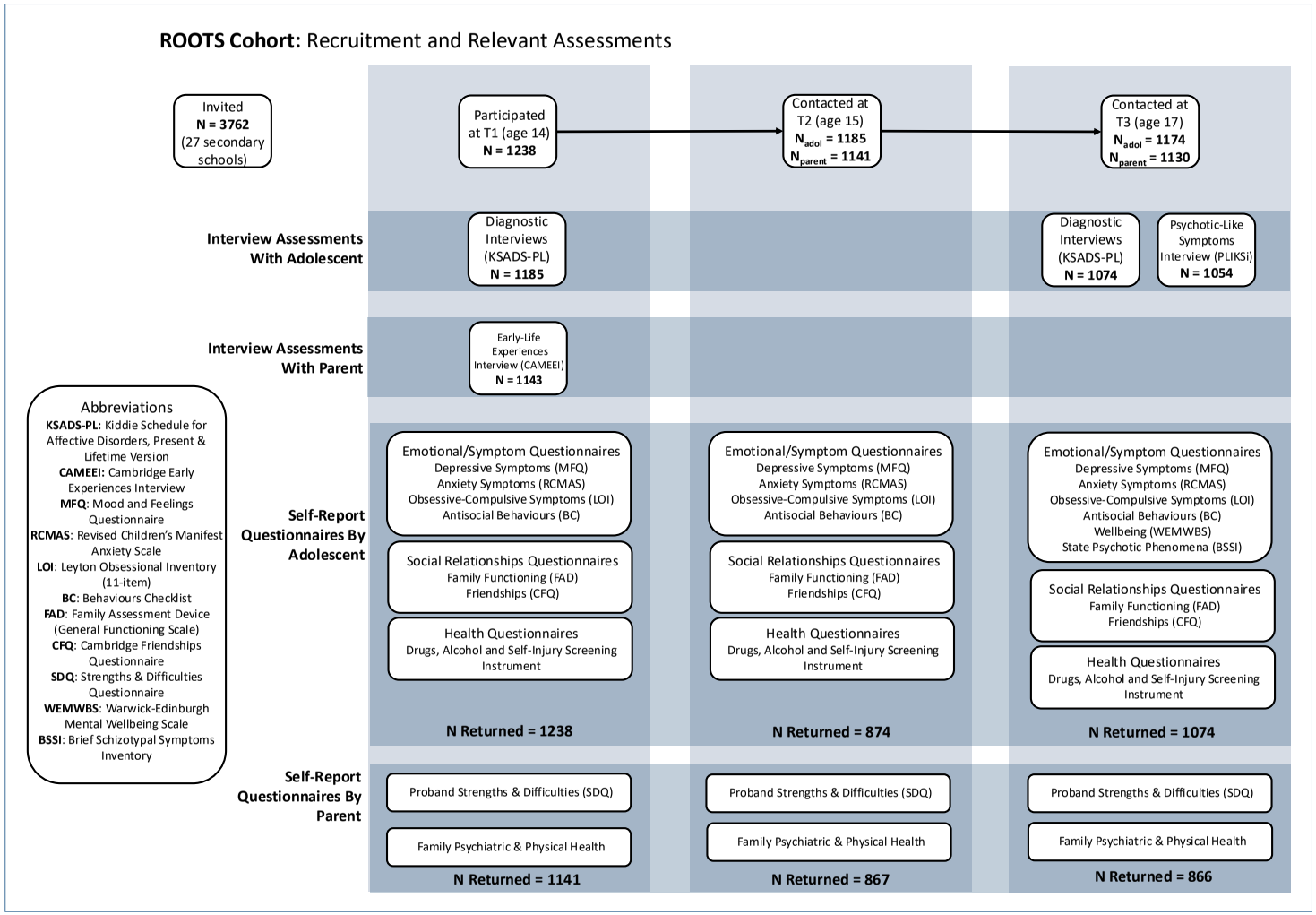


Figure 3.1: Recruitment and assessments in the ROOTS cohort. ROOTS is a longitudinal study of adolescent development. Participants were recruited by approaching 27 secondary schools in the country of Cambridgeshire. 18 schools agreed to take part and 3762 participants were invited. Of these, 1238 gave consent and entered the study. There were three main assessments, at age 14, 15.5 and 17. There was a further sub-study between the second and third time points investigating cognition.

in Figure 3.1. Self-reported questionnaire data were collected from adolescents, parents and teachers at each time point.

Sociodemographic information

Sociodemographic information was collected from parents at baseline. Socio-economic status (SES) was estimated from postcodes, using ACORN categories (http://www.caci.co.uk). The ACORN category of 'Hard-Pressed' was taken as a marker of low SES. Ethnicity and family history of mental illness were assessed.

Emotions/behaviours/symptoms

State depressive symptoms were measured using the Mood and Feelings Questionnaire (MFQ) (Costello and Angold, 1988). Anxiety symptoms were measured using the Revised Children's Manifest Anxiety Scale (RCMAS) (Reynolds and Richmond, 1978). Obsessive-compulsive symptoms were measured using the Leyton Obsessional Inventory (LOI, 11-item version) (Bamber et al., 2002). Antisocial behaviours were measured with an 11-item behaviours checklist (BC). At T3, state psychotic phenomena and social anxiety over the past 2 weeks were measured using the Brief Schizotypal Symptoms Inventory (BSSI) (Hodgekins et al., 2012) and wellbeing was measured using the Warwick-Edinburgh Mental Wellbeing Scale (Tennant et al., 2007) (WEMWBS). Distressing life events in the past year were measured using a life events questionnaire (LEQ).

Relationships with family and peers

At all time points, family functioning and support was measured using the General Functioning scale of the Family Assessment Device (FAD) (Epstein and Baldwin, 1983). Friendship quality and peer difficulties were measured using the Cambridge Friendships Questionnaire (CFQ) (van Harmelen et al., 2016). Drug use, alcohol intake and non-suicidal self-injury were assessed using a screening instrument. The Cambridge Early Experiences Interview (CAMEEI) (Dunn et al., 2011) was conducted with parents at T1 to investigate early-life experiences and exposure to childhood adversity.

Education and employment

At T3, number of secondary school qualifications (GCSEs) and educational/employment status were assessed.

Mental disorders and PEs

Semi-structured interviews were conducted with adolescents at T1 and T3. At T1 and T3, common mental disorders were assessed with the Kiddie Schedule for Affective Disorders, present and lifetime version (KSADS-PL) (Kaufman et al., 1997). At T3, discrete psychotic experiences over

the lifetime were measured using the Psychotic-Like Symptoms Inventory (PLIKSi) (Horwood et al., 2008).

Sub-studies

The ROOTS study also featured nested sub-studies investigating cognition, brain structure and brain function. Cognition was investigated in a sub-study between T2 and T3, when participants were aged approximately 16.5. The cognitive tasks assessed associative learning, behavioural inhibition and reversal learning in 273 participants were assessed at this time point. The sample was targeted to be enriched for exposure to childhood adversity, such that approximately half of the sample were exposed (Owens et al., 2012), as the focus of this study was interactions between genetic polymorphisms of the 5-HTTPLR and childhood adversity.

3.2.2 Neuroscience in Psychiatry Network (NSPN)

The NSPN 2400 cohort is an accelerated longitudinal cohort study designed to investigate behaviour and psychopathology, cognition and neurobiology over adolescence and young adulthood. The study is collaboration between the University of Cambridge and University College London, with the cohort recruited across both centres. The NSPN cohort study is ongoing. NSPN is supported by a strategic award by the Wellcome Trust (095844/Z/11/Z). Additional support was provided by the National Institute for Health Research Cambridge Biomedical Research Centre and the Medical Research Council (MRC)/Wellcome Trust Behavioural and Clinical Neuroscience Institute.

The study was designed to recruit a general population sample of people aged between 14-25. The study aimed to recruit roughly equal numbers of males and females in five equally-sized age groups: 14-15, 16-17, 18-19, 20-21 and 22-25.

The study involves assessments at up to three points: Baseline (BL), Follow-Up 1 (FU1) and Follow-Up 2 (FU2). A summary of the recruitment, time points and relevant assessments is shown in Figure 3.2. Self-reported questionnaire data were collected from participants using a postal Home Questionnaire Pack (HQP), with some filled in by parents if participants were under the age of 16.

The NSPN 2400 cohort was representative of England and Wales in terms of ethnicity (**% for England and Wales | % for NSPN 2400:** White: 82% | 78%; Mixed: 4% | 6; Asian: 9% | 10%; Black: 4% | 4%; Other 1% | %) and country of birth (**% for England and Wales | % for NSPN 2400:** UK birth: 87% | 85; non-UK birth: 13% | 15%). Parents of NSPN 2400 participants were less likely to have no qualifications and more likely to have undergraduate or higher degrees than the average for England and Wales ((**% for England and Wales | % for NSPN 2400:** No qualifications: 23% | 8%; Vocational qualifications: 4% | 3%; GCSE/A-level qualifications: 41% | 51%, undergraduate or higher degree: 27% | 38%). Socioeconomic deprivation was measured using the Index of Multiple Deprivation (https://www.gov.uk/government/collections/english-indices-of-deprivation). When the proportions of the NSPN 2400 cohort falling in each decile of socio-economic deprivation for England and Wales were calculated, each decile contained around 10% of the sample except the 1st decile, which was underrepresented and the 9th decile, which

Figure 3.2:Cohort diagram: NSPN

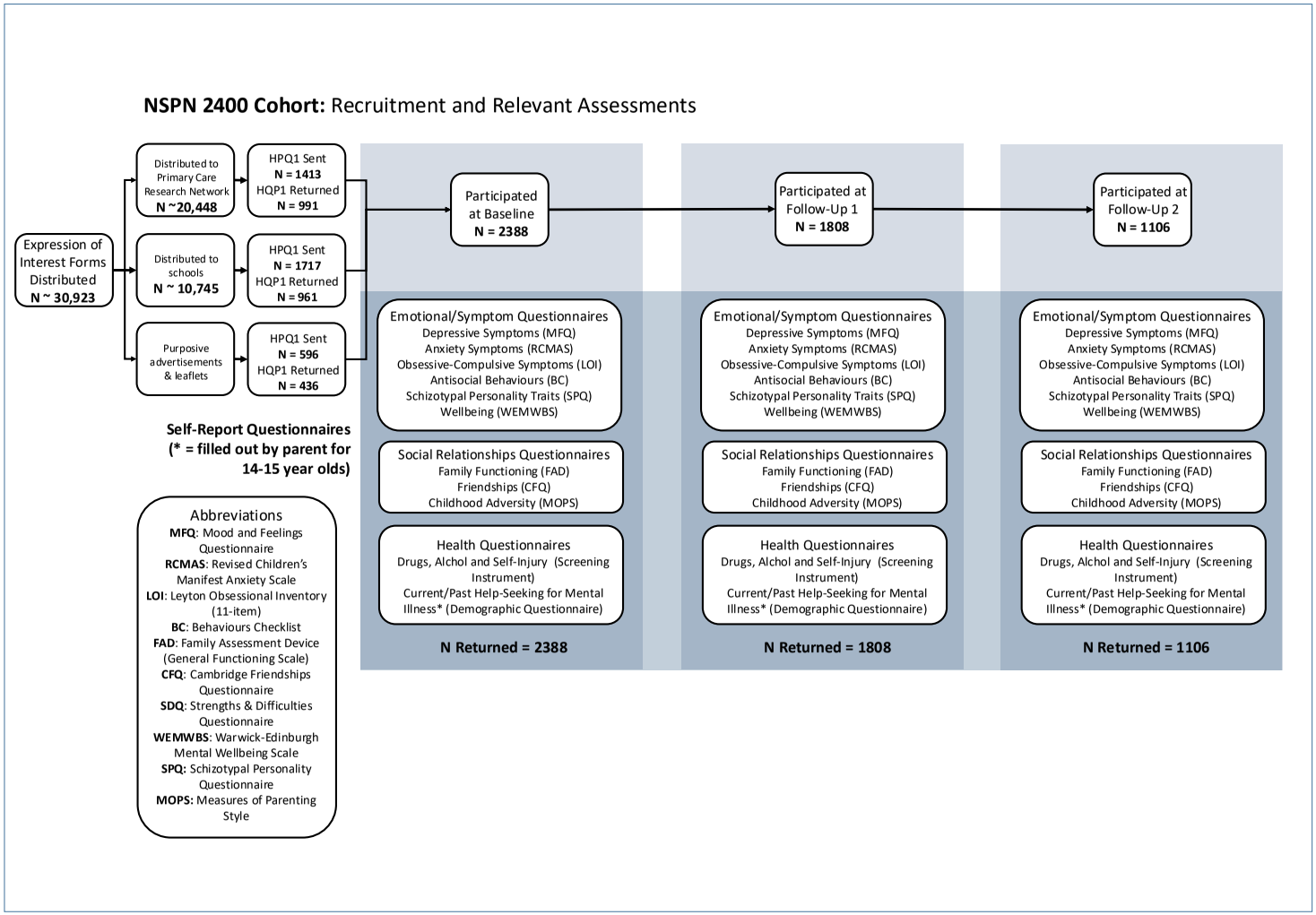


Figure 3.2: Recruitment and assessments in the NSPN 2400 cohort. NSPN is an accelerated longitudinal study of adolescent development. Participants were recruited through distribution of Expression of Interest forms via a primary care research network of GPs and to schools and purposive advertisements and leaflets. The study features three time points: Baseline, Follow-Up 1 and Follow-Up 2. Subsets of participants underwent additional cognition and brain imaging assessments.

was overrepresented (**Decile of deprivation | % of cohort:** 1 | 5%; 2 | 9%; 3 | 7%; 4 | 8 %; 5 | 9 %; 6 | 11%; 7 | 9%; 8 | 13%; 9 | 19%; 10 | 10%). Participants from Cambridgeshire came from less deprived areas than participants from London.

Participants expressed their interest to take part in the study using 'Expression of Interest' (EOI) forms. On receipt of the EOI form, if participants were still being recruited in that age/sex bin and the participant was eligible, the participant was sent the postal questionnaire pack. Participants returning the BL questionnaire pack formed the NSPN 2400 cohort.

To maximise representativeness, EOI forms were distributed through general practise surgeries using the NIHR Primary Care Research Network and local schools and further education colleges. Purposive advertisement through adverts and leaflets was also used. The median time between return of questionnaire packs was 1 year for BL to FU1, 823 days from BL to FU2 and 405 days from FU1 to FU2. Unless otherwise stated, the following instruments were assessed at each time point.

Sociodemographic information

Sociodemographic information was collected from participants (or from their parents, if the participant was younger than 16)at baseline. SES was estimated from postcodes, using the IMD. Ethnicity, years of parental education and family history of mental illness were assessed.

Emotions/behaviours/symptoms

Depressive symptoms (MFQ), anxiety symptoms (RCMAS), obsessive-compulsive symptoms (LOI), antisocial behaviours (BC), wellbeing (WEMWBS) were measured with the same instruments as in ROOTS. Schizotypy was measured using the Schizotypal Personality Questionnaire (SPQ, 74-item version) (Raine, 1991). Drug use, alcohol intake and non-suicidal self-injury were assessed using the same screening instrument as in ROOTS, the Drugs, Alcohol and Self-Injury Screening Instrument.

Relationships with family and peers

Family functioning (FAD) and friendship quality and peer difficulties (CFQ) were measured using the same instruments as in ROOTS. Parent-focused childhood adversity in the first 16 years of life was measured using the Measures of Parenting Style questionnaire (MOPS) (Parker et al., 1997).

Education and employment

Whether the participant was in full-time education, employment or unemployed was assessed.

Mental disorders

Current and past help-seeking or diagnoses for mental illnesses were assessed using simple self-report questions (reported by parents for participants younger than 16).

Sub-studies

The NSPN study featured a number of nested sub-studies. 300 participants (MRI cohort) underwent a series of structural and functional MRI assessments, a battery of behavioural tasks, IQ assessment and diagnostic interviews for mental disorders and PEs. A further at least 300 participants (Cognition cohort) will complete the battery of behavioural tasks, IQ assessment and diagnostic interviews. These participants will also be invited to provide blood and saliva samples for genetic analysis.

Due to the smaller size of this sample and limitations on data availability, I limited my investigations to data from the NSPN 2400 Cohort and did not use the data collected in the MRI or Cognition cohort.

3.3 Study design

Over the next 3 empirical chapters, I report studies designed to answer the 3 questions described at the beginning of this chapter. Due to the variety of methods and differences in relevant literature, I have expanded on relevant background, where necessary, and reported the methods in full in each chapter. I will not describe methods in this chapter.

In these studies, I utilised methods from psychometrics, latent variable modelling and data-driven clustering analyses. This work mainly uses cross-sectional data on symptoms, behaviours and potential aetiological factors. Following these studies, I selected a further set of questions to investigate using longitudinal data and behavioural tasks to which I could apply computational modelling.

Chapter 4

Properties of self-report instruments measuring psychotic phenomena

Abstract

Investigations into the dimensionality of instruments measuring psychotic phenomena and related schizotypal traits have produced divergent results and their measurement properties have rarely been systematically assessed in young people. I designed a validation pathway to assess the latent factorial structure and measurement properties of two schizotypy questionnaires, the Schizotypal Personality Questionnaire (SPQ) and the Brief Schizotypal Symptoms Inventory (BSSI), in two epidemiologically-principled general population cohorts of young people (age 17 or age 14-25). Dimensionality was assessed first by testing existing dimensional structures derived from the literature then, were those models inadequate, by model comparison of existing structures and novel structures generated using exploratory factor analysis. To assess measurement properties of individual schizotypy dimensions, I investigated their unidimensionality, internal consistency, measurement precision across levels of severity, systematic biases with sex and age (where possible) and reliability of sum scores to order participants by severity. I found that existing models of the dimensional structure of the SPQ either fit the data poorly or had redundant, non-distinct dimensions. A novel 6-factor solution outperformed novel and existing structures while maintaining distinct dimensions. All 6 dimensions were adequately unidimensional, had high internal consistency, had reasonable measurement precision over levels of severity, could be used reliably as sum scores and showed at least no bias in factorial structure over age and sex. These results support little advantage in using the 9 subscales of the SPQ and strongly question the validity of the three-factor and four-factor models that are often considered to be the basic structure of schizotypy. Existing three-factor models of the BSSI fit the data well. The BSSI scales were largely unidimensional, had high internal consistency and were strongly invariant over sex, though issues may arise due to rarity of some of the measured phenomena.

4.1 Research Questions

- What is the dimensionality of schizotypy and do existing models in the literature optimally describe empirical data when measured in young people?
- How reliably do self-report instruments measure PEs?

4.2 Introduction

In this chapter, I analysed the dimensionality and measurement properties of the two self-report instruments measuring PEs in the NSPN and ROOTS cohorts: the Schizotypal Personality Questionnaire (SPQ) (Raine, 1991) and Brief Schizotypal Symptoms Inventory (BSSI) (Hodgekins et al., 2012a).

Psychometrics is the field concerned with the quality of measurements of mental phenomena. It offers mathematical methods to estimate unobservable (i.e. 'latent') systems, often referred to as latent traits[1], that supposedly cause observations measured with instruments. Estimating and comparing structures of latent systems can test hypotheses on the dimensionality of unobservable systems. It also offers methods to estimate the precision with which an instrument measures the 'true' state of a system, like a person's true level of hallucination-proneness. This precision should modulate the extent to which empirical observations are relied upon to update and refine theories.

While there is not complete consensus, psychotic phenomena in the general population, particularly within the schizotypy field, are widely considered to comprise three systems (a 'three-factor model'): 'positive' or 'cognitive-perceptual' schizotypy, including anomalous perceptions and anomalous beliefs, 'interpersonal' or 'negative' schizotypy, including social difficulties, asociality and social anxiety, and 'disorganised' schizotypy, including odd speech and odd behaviours. It has been suggested that these domains map on to the dimensionality of clinical psychosis.

4.2.1 The Schizotypal Personality Questionnaire (SPQ)

The SPQ comprises 74 'true'/'false' statements and is one of the most widely used schizotypy questionnaires. It was originally intended to measure nine dimensions of schizotypal personality disorder, as of DSM-III (Association, 2013). Commonly, researchers investigating the structure of schizotypy have factor-analysed sum scores on these subscales, effectively identifying 'second-order' structures, with respect to the items measured.

There is not a consensus on the optimal dimensional structure of the SPQ. Studies have identified three-factor structures (Badoud, Chanal, Van Der Linden, Eliez, & Debbané, 2011; Bergman et al., 1996; Chen, Hsiao, & Lin, 1997; Fossati, Raine, Carretta, Leonardi, & Maffei, 2003; Raine et al., 1994; Reynolds, Raine, Mellingen, Venables, & Mednick, 2000; Vollema & Hoijtink, 2000; Wuthrich & Bates, 2006), four-factor structures (Compton, Goulding, Bakeman, & McClure-Tone, 2009; Fonseca-Pedrero et al., 2014; Stefanis et al., 2004) and a bifactor structure (Preti et al., 2015). This inconsistency is concerning and may arise because the nine original scales of the SPQ are themselves flawed, introducing measurement error. In support of this, the validities of the nine subscales and three/four-factor structures are questionable when estimated from item-level data (Chmielewski & Watson, 2008).

There are methodological issues with previous analyses of the SPQ. The subscale approach is convoluted, discards potentially valuable information measured at the item-level and means that the validity of second-order factors rests on the validity of the first-order subscales. Given the

[1]The term 'trait' is a convention and does not reflect that the system is stable over time

conceptual similarity and high correlations observed between these subscales, it is probable that some of the subscales are overlapping to the point of redundancy. Including multiple redundant items and/or subscales in analyses may introduce collinearity and artificial patterns of covariance, leading to spurious factors that do not represent 'true' variation with underlying mechanisms or aetiology. In particular, some scales tend to group together and may not practically be distinct, particularly Magical Thinking (MT) and Unusual Perceptual Experiences (UPE); Ideas of Reference (IoR) and Suspiciousness (Sus); Odd Speech (OS) and Odd Behaviour (OB); and No Close Friends (NCF) and Constricted Affect (CA) (Chmielewski & Watson, 2008). As a further limitation, the majority of work with the SPQ has used adult undergraduate samples, rather than community samples and samples with younger age ranges, when psychotic phenomena are more common but may not persist into adulthood (Zammit et al., 2013).

4.2.2 The Brief Schizotypal Symptoms Inventory (BSSI)

The BSSI comprises 20 statements with Likert-scale frequency responses with 5 categories indicating how often that statement has applied in the last two weeks ('Not at all', 'Occasionally', 'Sometimes', 'Often, 'All of the time'). The BSSI is based on the SPQ, with very similar if not identically worded items. It is designed to have three subscales: Paranoid Ideation (PI), with items from the SPQ Ideas of Reference and Suspiciousness scales; Anomalous Experiences & Beliefs (AEB – originally 'Anomalous Experiences' but not all items are strictly experiences), with items from the SPQ Magical Thinking, Unusual Perceptual Experiences and Ideas of Reference, and Social Anxiety (SA), with items from the SPQ Excessive Social Anxiety scale. To my knowledge, this instrument has only been used in two studies since its development (Freeman et al., 2015; Hodgekins et al., 2012b).

4.2.3 Analysis of factorial structure, or dimensionality

I investigated the dimensionality of the SPQ and the BSSI using factor analysis. Factor analytical approaches are a form of dimensionality reduction and are founded on the premise that covariance among groups of measured phenomena, labelled 'indicators' (e.g. questionnaire items), can be modelled as being caused by a smaller number of unobservable, 'latent', dimensions.

If dimensionality is poorly specified, it can introduce error into measurement. Dimensional structures might have various problems. A dimensional structure may fit the item-level data poorly, suggesting its dimensions do not capture empirical data well. Instruments can have spurious dimensions that perform well psychometrically but have little validity, usually caused by items that are re-phrasings of each other. Instruments can have items that are included in dimensions but are poorly related to the overall constructs or to other items, adding noise. Dimensions can have very few numbers of items, which makes their measurement unreliable as it relies more on each noisy individual item. Dimensions can be very highly related to one another to the point of redundancy, suggesting they do not truly have separate mechanisms or aetiologies. Finally, the complexity of dimensions may be lost in reducing their composite items to a summary label, such as 'Suspiciousness'.

I set out to validate the existing factorial structures of dimensions of the SPQ and the BSSI to see

Figure 4.1: Dimensionality analysis pathway

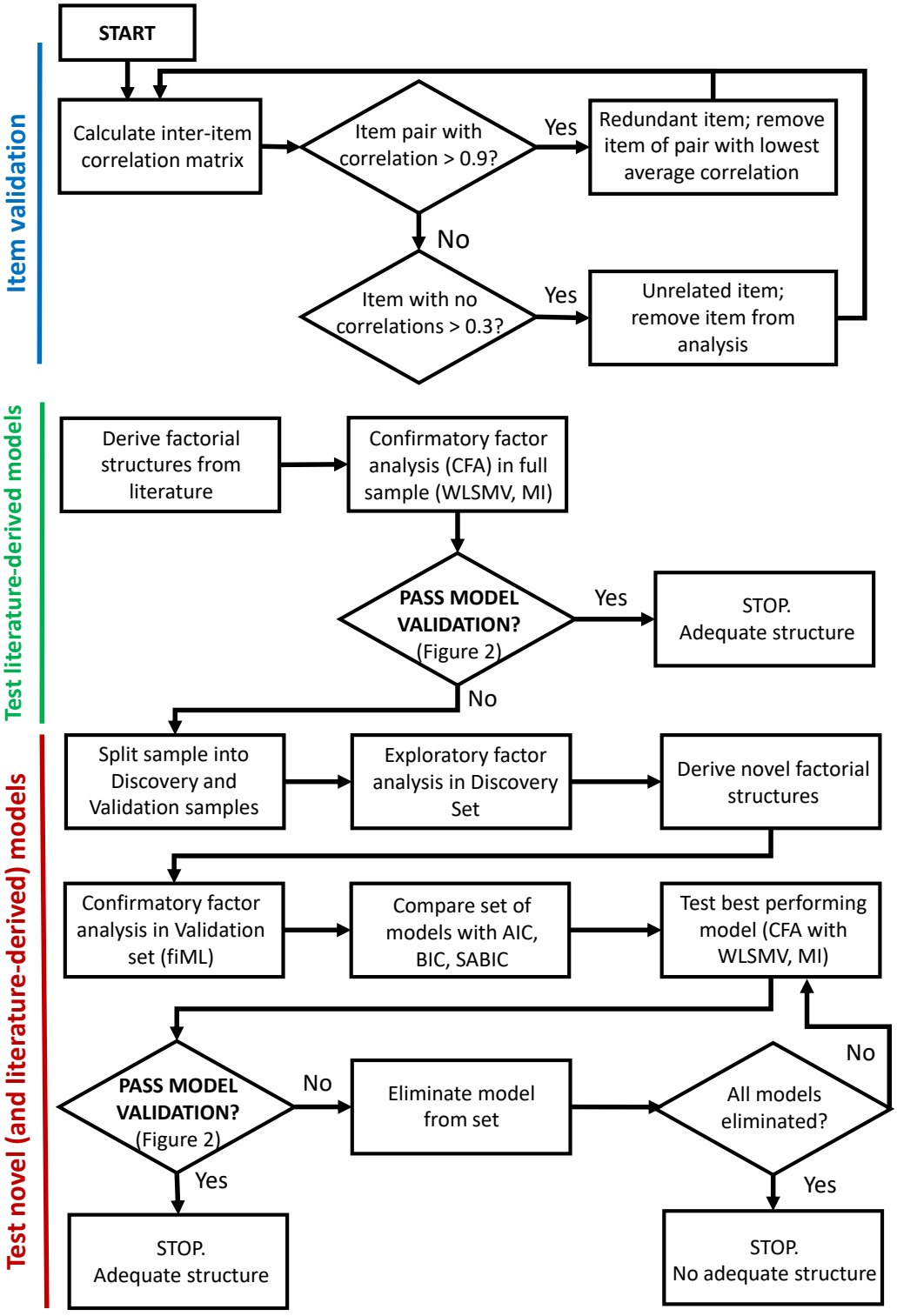


Figure 4.1: Flowchart of dimensionality analysis pathway. The pathway can be divided into three stages: 1) validation that items are distinct but moderately related to other items, 2) validating dimensional models derived from the literature and 3) comparing and validating novel dimensional models, if literature-derived models are inadequate.

Figure 4.2: Validation of dimensional models

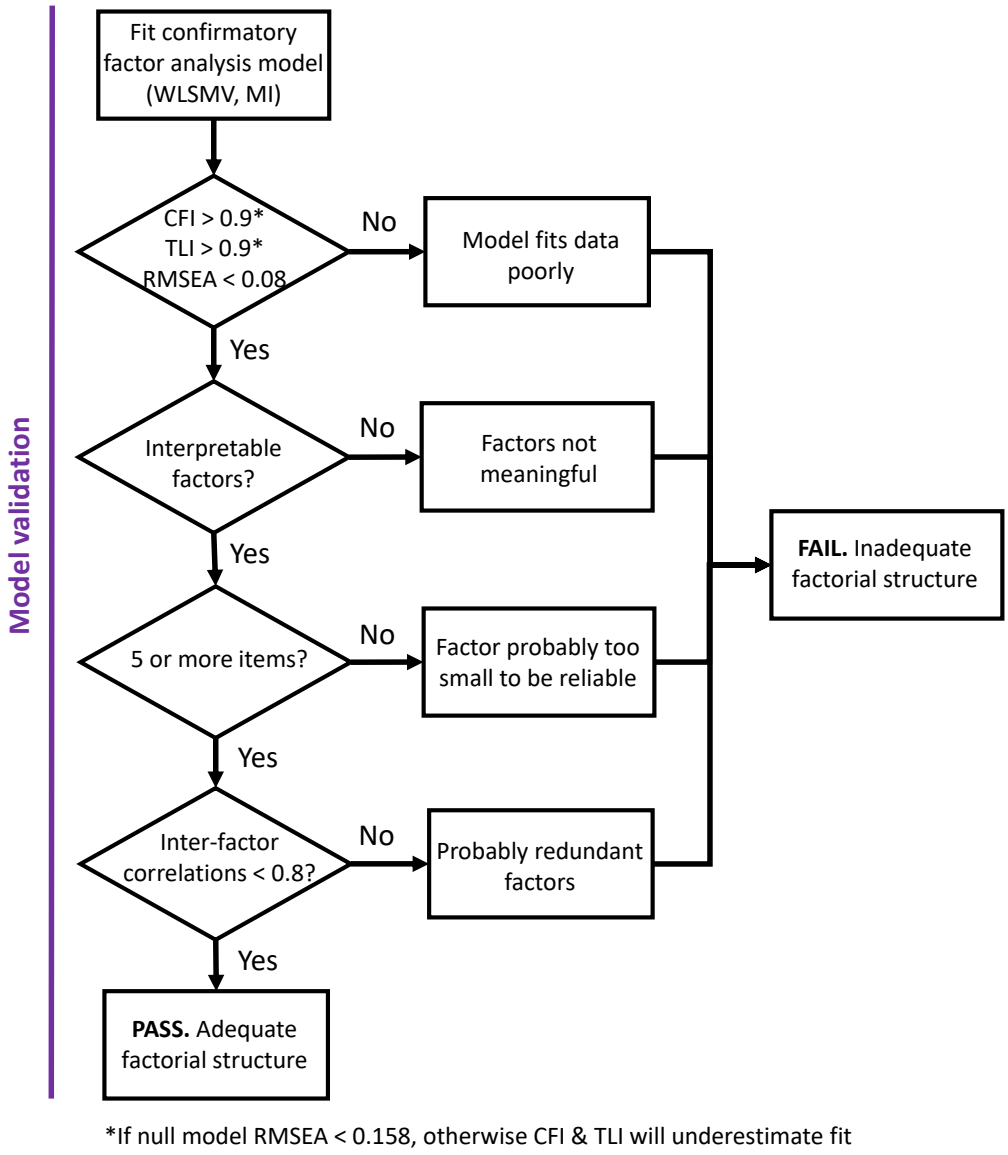


Figure 4.2: Flowchart of validation of dimensional models. The pathway was designed to test whether a dimensional model fit the data well, had interpretable factors, had factors with enough items to be used as standalone instruments and had factors that were likely to be meaningfully distinct.

whether their dimensions displayed any of these problems and, if so, to attempt to derive novel factorial structures that mitigated those problems. The analysis pathway is shown in Figure 4.1.

The pathway was designed to identify an 'optimal' factorial structure that: 1) was estimated from a pool of items that were all distinct but at least moderately-related to one another; 2) showed sufficient goodness of fit to item-level data and 3) had distinct, interpretable dimensions with enough items to be reliable (at least 5) (see Figure 4.2).

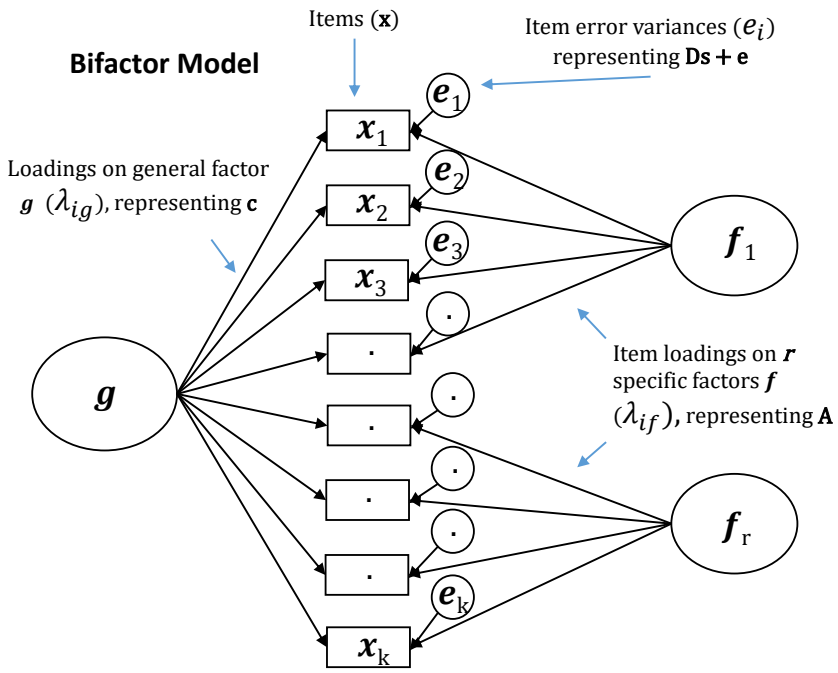
4.2.4 Measurement properties

I then assessed the measurement properties of all dimensions in the optimal factorial structure. Estimating the reliability of a scale is challenging, and reliability is a term used loosely, particularly in applied psychology research. Most applied research discusses 'internal consistency' of scales, which can be estimated from a single set of measurements made with an instrument. However, internal consistency means different things to different researchers (Revelle & Zinbarg, 2009; Sijtsma, 2009). Using terms suggested by Revelle & Zinbarg (2009) (Revelle & Zinbarg, 2009), I investigated the following set of properties:

1. **Unidimensionality**, or whether a dimension is truly measuring one thing.
2. **Homogeneity**, or the proportion of variance in observed measurements that is caused by one factor. This helps assess how appropriate it is to use sum scores on an instrument.
3. **Internal consistency**, or the upper bound on the variance in observed measurements that is not due to noise. In effect, this is the greatest meaningful correlation that could be achieved between the dimension and other variables.
4. **Measurement precision across all severity/intensity levels.** This is important to know whether measurements become less reliable in people with higher or lower scores.
5. **Systematic biases caused by other factors.** This is important to know whether factors like age or sex will bias results.
6. **Appropriateness of sum scores to rank participants by severity/intensity.** This is important as instruments are almost always used as sum scores in empirical studies.

Properties 1-3 can be estimated using hierarchical latent factor modelling (Figure 4.3). Properties 4 and 6 can be estimated using parametric and nonparametric item response theory (IRT) analysis, respectively. IRT analyses define mathematical functions of how different levels of a latent trait will translate into different observed responses on items, known as 'item response functions' (IRFs, Figure 4.4). Property 5 can be investigated using latent variable modelling across different groups of interest.

Figure 4.3 Hierarchical latent variable modelling approaches to estimating reliability



Hierarchical-factor modelling approach to reliability

$$\boldsymbol{x} = \boldsymbol{cg} + \boldsymbol{Af} + \boldsymbol{Ds} + \boldsymbol{e}$$

$\boldsymbol{x}$ is the k x 1 vector of observed scores on the k items
g is a general factor common to all items
$\boldsymbol{c}$ is a k x 1 vector of loadings on the general factor
$\boldsymbol{f}$ is an r X 1 vector of specific factors
$\boldsymbol{A}$ is the k X r matrix of loadings on the specific factors
$\boldsymbol{s}$ is the k x 1 vector of specific factors unique to each item
$\boldsymbol{D}$ is the k X k diagonal matrix of loadings on the item specific factors
$\boldsymbol{e}$ is the k x 1 vector of residual or error item variances.

Calculating Omega (ω) statistics

ω_H: proportion of variance attributable to one factor

$$\omega_H = \frac{Sum\ of\ squared\ loadings\ on\ \boldsymbol{g}}{Sum\ of\ squared\ loadings\ on\ \boldsymbol{g}, \boldsymbol{f_r} + error\ variances}$$

ω_T: upper bound on reliability

$$\omega_T = \frac{Sum\ of\ squared\ loadings\ on\ \boldsymbol{g}, \boldsymbol{f_r}}{Sum\ of\ squared\ loadings\ on\ \boldsymbol{g}, \boldsymbol{f_r} + error\ variances}$$

Figure 4.3: Variance in a test can be partitioned into four components. These are a general factor (g), explaining covariance in all items (i), r specific factors (f) explaining additional covariance among some items, a specific factor (s) for each item that explains unique measurement variance for that item, and measurement error or noise (e). This model can be estimated from observed data as a 'bifactor' model. This model has a general factor that explains some variance in all items and specific factors that explain variance in smaller groups of items. For purposes of model identifiability, the specific factors are often constrained to be orthogonal to the general factor. This model assumes uncorrelated factors and factor errors, and that the variances of all latent factors are fixed to 1. With this approach we can estimate ω_{H} and ω_{T}.

Figure 4.4 Item response theory (IRT) analyses

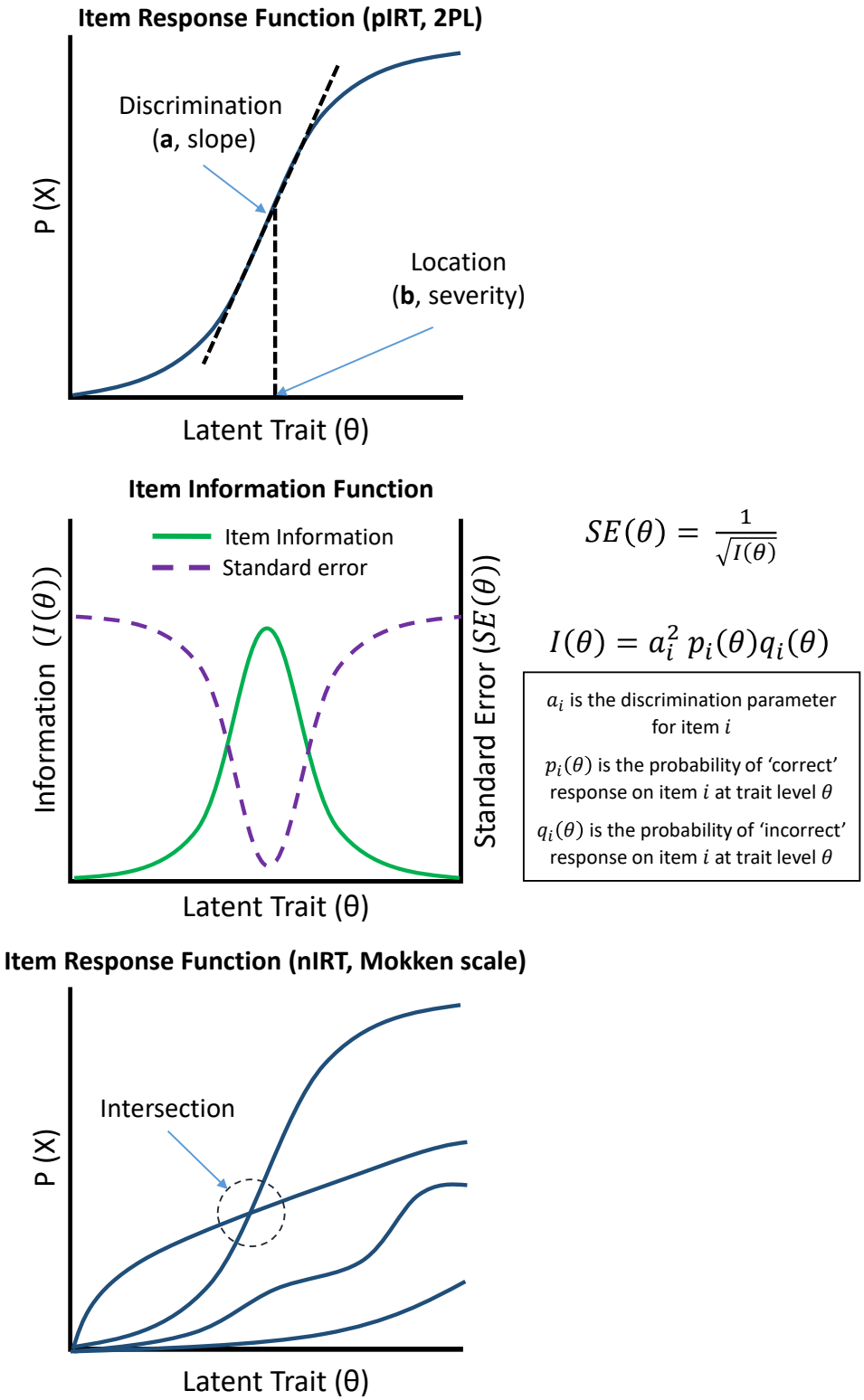


Figure 4.4: Item response theory analysis (IRT). A) An item response function (IRF) described by two-parameters of a logistic curve (2PL). B) Parametric IRT can be used to quantify where on the trait distribution each item measures in terms of information contributed. Due to the assumption that items are locally independent, IRFs and information is additive and can be used for single items or whole scales. C) IRFs estimated empirically using Mokken scaling. This can be used to investigate whether sum scores order participants correctly by the latent trait.

4.3 Method

4.3.1 Data

Data on the SPQ come from the NSPN baseline assessment only. The SPQ formed part of the postal questionnaire pack sent to the NSPN 2400 cohort. At time of analysis, 2388 participants returned questionnaire packs. Data on the BSSI come from the ROOTS cohort at time 3 only. The BSSI formed a part of a postal questionnaire pack. For further details on the cohorts, see Methodology. Of the 1238 participants who entered the study at time 1, 1054 took part at time 3 and 966 completed the BSSI. All analyses were performed using R for Statistical Computing (R Core Team, 2016).

4.3.2 Investigating dimensionality

Ensuring items were distinct but moderately-related to other items

I ensured items were distinct but moderately related to other items by examination of inter-item correlation matrices. Items were considered not distinct if they had any inter-item correlations exceeding 0.9. Items were considered unrelated to other items if they had no inter-item correlations of at least 0.3. I used a step-wise procedure in which offending items were identified, the one with the lowest average inter-item correlation removed, and the correlation matrix re-estimated. I performed this procedure for non-distinct and for unrelated items separately, till no such items remained. To accommodate categorical item-level data, I used polychoric (for the multi-level ordinal responses on the BSSI) and tetrachoric (for the binary responses on the SPQ) correlation matrices.

Literature-Derived Dimensional Structures

I generated a set of item-level models from currently-used models of the SPQ and the BSSI. Cross-loadings were not allowed. When studies reported second-order structures in which subscales cross-loaded on to multiple second-order factors, I generated all possible combinations of model structures in which the cross-loading item loaded on to one of those factors.

Choice of factor analysis model estimator

Specialised robust estimation methods, like diagonally weighted-least-squares, mean- and variance adjusted (WLSMV), exist for estimating latent variable models from categorical data. These may be more appropriate than traditional maximum likelihood (ML) methods as they estimate polychoric correlations. For analyses not involving comparison of two or more models, I used a WLSMV estimator. All models were fit using the *lavaan* (Rosseel, 2012) package, supported with functions from *psych* (Revelle, 2014) and *semTools* (semTools Contributors, 2016).

Goodness of fit

I assessed fit of WLSMV-estimated models using two robust versions of CFI and TLI, which should both exceed 0.9 and preferably 0.95, and a robust version of RMSEA, which should not exceed 0.8 and preferably 0.5.

Distinct, sufficiently large and interpretable dimensions

These properties were assessed from factor models fit using WLSMV-estimated models. Factors were declared distinct if no inter-factor correlations exceeded 0.8. Factors were sufficiently large if they had at least 5 items. Items loading on each factor were examined for whether the whole factor was interpretable.

Novel Factorial Structures

If no model structures based on the literature met the above criteria, I proceeded to define novel model structures using exploratory factor analysis (EFA). I randomly split the sample into an equally sized 'Discovery' set and 'Validation' set, preserving the proportions of male and female participants and, for NSPN, participants in different age bins (14-16, 17-18, 19-20, 21-22, 22-25).

EFA estimates loadings on a given number of latent factors, from which model structures can be identified. I estimated EFA solutions with 1 to 9 factors, using a 'minres' estimator and 'oblimin' rotation with the 'psych' package (Revelle, 2014), allowing for correlated factors. Model structures were generated by setting each item to load on to its highest loading factor, with no cross-loading allowed. No items were removed to preserve the same pool of items across all models for model comparison.

All novel and literature-derived models were then fit to the Validation set, using a robust maximum likelihood estimator (MLR), with missing values estimated using full-information maximum-likelihood (fiML). Log-likelihood based fit indices, the AIC, BIC and SABIC were used for model comparison because they trade-off model fit and model parsimony; lower values indicate a better-performing model. I selected the best performing model that measured broadly interpretable domains and had at least 5 items per factor. I re-estimated that model in the Validation set and full dataset with a WLSMV estimator to examine goodness of fit, factor distinctness, size and interpretability (Figure 4.2). If the model did not meet these criteria, I moved on to the next best-fitting model according to AIC, BIC and SABIC until an adequate model was found.

4.3.3 Investigating measurement properties of individual scales

Once adequate dimensions had been identified, I examined their measurement properties independently.

Unidimensionality

I investigated unidimensionality by attempting to fit a bifactor model to scale items that were supposedly measuring a single factor. Adequate fit of the bifactor model indicates that there is some variance common to all items that can be explained by a single factor.

Homogeneity

I quantified how much variance is caused by a single factor by calculating the proportion of variance in the observed measurements explained by the general factor in a bifactor model (Figure 4.3). This value is McDonald's coefficient Omega (McDonald, 1978) (ω), which Zinbarg et al., relabelled as 'Omega Hierarchical' (Zinbarg, Revelle, Yovel, & Li, 2005) (ω_{H}). ω_{H} gives an index of how 'homogenous' an instrument is and how useful sum scores of that instrument will be. It is recommended that ω_{H} must exceed 0.5 if sum scores for an instrument are to be used.

Internal consistency, or upper bound on reliability

Due to limitations on our theories and measurements, no instrument will ever be perfectly unidimensional. However, variance that is not associated with a single dimension is not necessarily noise. We can estimate the proportion of variance that is non-noise, which would be the highest meaningful correlation we should expect to make with other instruments, or the 'greatest upper bound' on reliability.

I approximated the proportion of variance in observed measurements explained by the general factor and additional specific factors (Figure 4.3). This value is McDonald's coefficient 'Omega Total' (McDonald, 1999) (ω_{T}) and is an upper bound on the reliability (Revelle & Zinbarg, 2009). It is an estimate of the maximum meaningful correlation we should be able to identify between the system in question and another system, and Revelle & Zinbarg (Revelle & Zinbarg, 2009) suggest this is used to indicate 'internal consistency'

Measurement precision across severity/intensity levels

It is important to know whether an instrument can measure the full distribution of the latent trait with reasonable accuracy. Uneven measurement precision across the trait distribution means that measurement may be systematically less reliable in certain people. This can reduce power to detect associations and produce spurious associations, such as when an instrument is used to calculate change scores over time (Reise & Haviland, 2005). This may be particularly relevant for psychopathology research, in that many symptom instruments measure high levels of symptoms accurately but low levels of symptoms inaccurately (Reise & Waller, 2009).

I investigated measurement precision across the latent trait using pIRT. I fit two-parameter logistic (2PL) IRT models to the items for each scale and calculated item information distributions that indicated what severity of the latent trait the item could measure (4.4). I fit 2PL pIRT by expectation-maximization (EM) with the Newton-Raphson method using the *mirt* (Chalmers, 2012) package.

Systematic biases caused by other characteristics

Systematic biases can occur when different groups, like men and women, tend to interpret items in a different way. We refer to this as a failure of 'measurement invariance' or the presence of 'differential item functioning', for specific items. I tested this property by fitting multi-group latent variable models with increasingly strict constraints that model parameters must be equal across groups. Significantly poorer fit when models are constrained to be equal indicates failure of measurement invariance.

Increasingly strict equality constraints were imposed such that the item loadings (weak invariance), then also item thresholds (strong invariance), then also item residuals (strict invariance) were equal across groups. I tested change in model fit by the difference in the CFI. A change in CFI (ΔCFI) of -0.01 or a greater decrement was taken to indicate failure of invariance. For dichotomous items, such as those in the SPQ, residual variances must be constrained to 1 to ensure model identifiability, so I tested only weak and strong invariance.

In ROOTS and NSPN, I tested invariance over sex. In NSPN, I also tested invariance over age, as the sample aged between 14-25. Age was split into two age bins: adolescents aged 14-17, and young adults aged 18-25. Models were fit with a WLSMV estimator to complete cases data.

Appropriateness of sum scores to rank participants by severity/intensity

Sum scores are, by far, the most common use of psychometric instruments like the SPQ and the BSSI. Sum scores give every item equal weighting, and if people with different levels of a system do not all interpret the items as having the same rank order of severity, the sum score may misorder people in terms of their 'true' system values (Figure 4.4). If items are ranked in terms of severity in the same way by all participants, they form a hierarchy and this property is known as 'invariant item ordering'. The presence of invariant item ordering indicates that sum scores are a reliable way to measure a continuously varying system in a population.

I investigated invariant item ordering using Mokken scaling, which estimates the full IRF empirically rather than summarising it parametrically. I tested whether a Mokken scale fits the data and whether any of the item-response functions (IRFs) significantly intersected, indicating that the severity ranking of items is not the same over all participants. The number of items that do not have intersecting IRFs was calculated and the strength of IIO estimated with parameter HT. HT > 0.3 indicates at least weak IIO and presence of a hierarchy, strengthening the use of sum scores.

I report the scalability coefficient for the instrument, H (Loevinger, 1947), which is a measure of 'homogeneity' and indicates how strongly the items form a Mokken scale, which supports use of sum scores. H values > 0.3 indicate that the items form a weak Mokken scale, H > 0.4 indicates a moderate Mokken scale and H > 0.5 indicates a strong Mokken scale. Recent extensions of Mokken scaling show that it is possible to directly measure 'manifest invariant item ordering' (Ligtvoet et al., 2010) and indicate the strength of any hierarchies with coefficient HT. I used a backwards step-wise item selection procedure to remove items that have intersection IRFs

and calculated HT from any remaining, invariantly ordered items. HT gives an indication of the accuracy of invariant item ordering: HT > 0.3 indicates low, but acceptable hierarchical ordering, HT > 0.4 indicates moderate hierarchical ordering and HT > 0.5 indicates strong hierarchical ordering. Mokken scales were fit to the data using the *Mokken* (van der Ark, 2007) package for R.

4.3.4 Missing Data

Using only complete cases is a suboptimal strategy for dealing with missing data, if that missing data is not missing completely at random (MCAR). If data is missing at random (MAR), missingness depends on other measured factors such as age or sex. Ignoring MAR data (or data missing not at random, where missingness depends on unmeasured factors) can introduce bias into analyses. This bias can be reduced using methods that estimate MAR data. In checking assumptions of MAR and reporting results of analyses using missing data, I followed recommendations by (Sterne et al., 2009).

For factor analyses, I used two strategies for dealing with MAR data, depending on the estimator used to fit models to data and purpose of the analysis. A full-information ML (fiML) estimator was used for model comparisons as it allows computation of appropriate comparative fit indices based on log-likelihood (e.g. AIC, BIC, SABIC). A WLSMV estimator with 25 multiply imputed data sets was used to assess fit of individual models because it is more appropriate for categorical indicators and robust to non-normal variables. Imputed values were generated using predictive mean matching, with auxiliary variables included to improve the plausibility of imputations (Table 4.1). For measurement invariance, pIRT and nIRT analyses I used complete-cases data only.

4.4 Results

4.4.1 SPQ

Missing data: SPQ

Table 4.1: Missing data for the SPQ in NSPN. The missing values were judged to meet missing-at-random (MAR) assumptions so were suitable for multiple imputation and estimation using full-information maximum-likelihood.

Reporting Guideline	Description
Number of missing values for variables of interest	2388 filled in SPQ. 2106/2388 had complete data (88.1% of filled in questionnaire. 45 partially complete questionnaires had more than 5 items missing.

Table 4.1 – continued from previous page

Possible reasons for missingness	Higher psychopathology, sociodemographic features (e.g. sex, low socioeconomic status)
Differences in key exposures and outcomes of interest in missing and observed data	Logistic regressions were used to predict having incomplete data on the BSSI from other variables (see ?Auxiliary variables used in imputation procedure? below). Numbers in brackets indicate OR and 95% CI. Incomplete data was predicted by: male sex (1.9, 1.47 - 2.46), low socioeconomic status (1.95, 1.38 - 2.75), years of maternal education (0.92, 0.87 - 0.98), lifetime PEs (1.67, 1.03 - 2.64), and childhood adversity (1.74, 1.31 - 2.30).
Assumptions about missing data?	Missing at random (MAR)
Imputation software	Predictive mean matching (PMM), *Hmisc* package, R for statistical computing
N imputed datasets	25
Auxiliary variables used in imputation procedure	Non-white ethnicity, SES, years of mother's education after age 16, family history of psychiatric disorder, lifetime, past-year and persistent psychotic experiences measured using the Psychotic-Like Symptoms Interview (Horwood et al., 2008) nonpsychotic disorders measured with the K-SADS-PL (Kaufman et al., 1997) (occurring before age 14, at age 14 and at age 17, age 14), childhood adversity between 0-14 measured with the CAMEEI (Dunn et al., 2011), age 17 item-level responses about depressive symptoms (MFQ) (Angold et al., 1995), age 14 and age 17 self-report anxiety symptoms (RCMAS) (Reynolds and Richmond, 1997), obsessive-compulsive symptoms (LOI) (Berg et al., 1986; Bamber et al., 2002), antisocial behaviours (BC) (Cousins et al., 2016), friendship quality (CFQ) (van Harmelen et al., 2016) family support (FAD) (Epstein and Baldwin, 1983) and age 17 self-report wellbeing (WEMWBS) (Tennant et al., 2007).
Approach to non-normal and categorical variables	PMM preserves the distribution of observed variables by borrowing real values from observed data that could plausibly be the missing value
Interactions	None included

Table 4.1 – continued from previous page

Plausibility of observed and imputed values	Visual inspection showed very similar distributions of distributions of observed and imputed values
Plausibility of MAR assumption supported by variables included in imputation model?	Logistic regressions confirmed that missingness on individual BSSI items was predicted by one or more of the imputation variables (see "Auxiliary variables used in imputation procedure").
Complete cases analyses	I also reported complete cases analyses
Sensitivity analyses	Sensitivity analyses for investigating dimensionality with missing data are complex, e.g. "do the participants with missing data have three dimensions of schizotypy, rather than six?" Possible sensitivity analyses might impute sets of missing data that were most-like or least-like the set of factorial structures tested and estimate the variability in winning dimensional structures. Given this complexity and the high proportion of complete data, I chose not to conduct sensitivity analyses, though these might be important future investigations.

The SPQ missing data was judged to be plausibly MAR (Table 4.1).

Redundant and Unrelated Items

One pair of items from the 'Suspiciousness' scale had a correlation coefficient of 0.93 ("18: Do you often feel that others have it in for you?" and "59: I often feel that others have it in for me"). Item 18 had the lowest average correlation with all other items (Item 18: average correlation = 0.398; Item 59: average correlation = 0.404) and was removed from subsequent analyses. On re-estimation of the correlation matrix, no item correlations exceeded 0.9.

Item 49, "Writing letters to friends is more trouble than it is worth", showed no inter-item correlations over 0.3 and was removed from subsequent analyses. On re-estimating the correlation matrix, no other items had no correlations over 0.3. The remaining 72 items were used as the final item pool.

Literature-Derived Dimensional Structures

I derived model structures from the three-factor (Raine et al., 1994) and four-factor (Stefanis et al., 2004) models that have been most widely replicated in the literature (Table 4.2).

All models converged normally when fit to 25 imputed datasets. However, no three-factor or four-factor structure showed acceptable values of CFI and TLI (Table 4.3). By comparison, Raine's

Table 4.2: Models of the SPQ derived from prominent existing models in the literature (Raine, 1991 and Stefanis et al., 2004). Both models feature cross-loadings, which reduce factor interpretability and may cause undue influence of a few items in the overall model. I constructed all possible model combinations with no cross-loadings.

Scale	IoR	ESA	MT	UPE	OB	NCF	OS	CA	SUS
Raine 3F A	CP	IP	CP	CP	Dis	IP	Dis	IP	CP
Raine 3F B	CP	IP	CP	CP	Dis	IP	Dis	IP	IP
Stefanis 4F A	Para	Para	CP	CP	Dis	IP	Dis	IP	Para
Stefanis 4F B	Para	IP	CP	CP	Dis	IP	Dis	IP	Para
Stefanis 4F C	Para	Para	CP	CP	Dis	IP	Dis	IP	IP
Stefanis 4F D	Para	IP	CP	CP	Dis	IP	Dis	IP	IP

9-factor model did show acceptable CFI and TLI. However, some factors showed some very high inter-factor correlations (Inter-factor correlations: Ideas of Reference & Suspiciousness = 0.86; Unusual Perceptual Experiences & Magical Thinking = 0.80, No Close Friends & Constricted Affect = 0.95), suggesting these domains are not truly distinct. Full parameter estimates of the original 9-factor model fit to the imputed datasets are given in Appendix B. I proceeded to generate novel factorial structures using EFA.

Table 4.3: Fit indices of literature-derived dimensional structures of the SPQ (WLSMV, 25 imputed datasets). Only Raine's (1991) 9-factor model showed adequate fit to the data. However, some of the model's factor correlations exceeded 0.8, so may not be truly distinct. This model therefore does not meet my validation criteria.

Model	CFI	TLI	RMSEA	RMSEA (Lower 95% CI)	RMSEA (Upper 95% CI)
Raine 3F A	0.864	0.86	0.045	0.045	0.046
Raine 3F B	0.84	0.835	0.049	0.048	0.05
Stefanis 4F A	0.839	0.834	0.049	0.049	0.05
Stefanis 4F B	0.877	0.873	0.043	0.042	0.044
Stefanis 4F C	0.831	0.826	0.05	0.05	0.051
Stefanis 4F D	0.847	0.842	0.048	0.047	0.049
Raine 9F	0.911	0.907	0.037	0.036	0.038

Novel Dimensional Structures

Table 4.4 – continued from previous page

Item	Original Scale	EFA 1F	EFA 2F	EFA 3F	EFA 4F	EFA 5F	EFA 6F	EFA 7F	EFA 8F	EFA 9F
15	NCF	1	1	1	1	3	1	1	1	4
16	OS	1	2	3	3	1	5	7	6	6
17	CA	1	1	1	1	3	1	1	1	4
19	IoR	1	2	3	3	5	3	4	7	8
20	ESA	1	1	1	4	4	4	2	3	1
21	MT	1	2	2	2	2	2	6	7	8
22	UPE	1	2	2	2	2	2	5	5	5
23	OB	1	2	3	3	1	6	3	2	2
24	NCF	1	1	1	1	3	1	2	3	1
25	OS	1	2	2	4	1	5	7	6	6
26	CA	1	1	1	1	3	1	1	1	4
27	Sus	1	2	2	4	5	3	4	4	3
28	IoR	1	2	2	2	2	2	6	7	8
29	ESA	1	1	1	1	4	4	2	3	1
30	MT	1	2	2	2	2	2	5	5	5
31	UPE	1	2	2	2	2	2	6	8	9
32	OB	1	2	3	3	1	6	3	2	2
33	NCF	1	1	1	1	3	1	1	1	4
34	OS	1	2	3	3	1	5	7	6	6
35	CA	1	1	1	1	3	1	1	1	4
36	Sus	1	1	3	1	3	3	1	1	4
37	IoR	1	2	2	2	2	2	6	7	8
38	ESA	1	1	1	1	4	4	2	3	1
39	MT	1	2	2	2	2	2	5	7	8
40	UPE	1	2	2	2	2	2	5	5	5
41	NCF	1	1	1	1	3	1	1	1	4
42	OS	1	1	3	1	3	1	1	1	7
43	CA	1	1	3	1	3	1	1	1	2
44	Sus	1	2	2	4	5	3	4	4	3
45	IoR	1	2	2	4	5	3	4	4	3
46	ESA	1	1	1	1	4	4	2	3	1
47	MT	1	2	2	2	2	2	5	5	5
48	UPE	1	2	3	2	2	3	1	1	5
50	OS	1	2	3	3	1	6	6	2	2
51	CA	1	1	1	1	3	1	1	1	4
52	Sus	1	1	1	1	3	1	1	1	4
53	IoR	1	2	2	4	5	3	4	4	3
54	ESA	1	1	1	1	4	4	2	3	1
55	MT	1	2	2	2	2	2	5	5	5
56	UPE	1	2	2	2	2	2	5	5	5
57	NCF	1	1	1	1	4	1	2	3	1
58	OS	1	2	3	3	1	5	7	6	6
59	Sus	1	2	2	4	5	3	4	4	3
60	IoR	1	2	2	4	5	3	4	4	3
61	UPE	1	2	2	2	2	2	6	8	9
62	NCF	1	1	1	1	3	1	1	1	8
63	IoR	1	2	2	4	5	3	4	4	3

Table 4.4 – continued from previous page

Item	Original Scale	EFA 1F	EFA 2F	EFA 3F	EFA 4F	EFA 5F	EFA 6F	EFA 7F	EFA 8F	EFA 9F
64	UPE	1	2	2	2	2	2	6	8	9
65	Sus	1	2	2	4	5	3	4	1	4
66	NCF	1	1	1	1	3	1	1	1	4
67	OB	1	2	3	3	1	6	3	2	2
68	CA	1	1	1	1	3	1	1	1	7
69	OS	1	1	1	1	1	1	1	1	7
70	OB	1	2	3	3	1	6	3	2	2
71	ESA	1	1	1	1	4	4	2	3	1
72	OS	1	2	3	3	1	5	7	6	6
73	CA	1	1	1	1	3	1	1	1	4
74	OB	1	2	3	3	1	6	3	2	2

Table 4.4 shows the structures of the models derived from EFA. Figure 4.5 shows the AIC, BIC and SABIC values for all novel and literature-derived models, in order of BIC values. Importantly, all novel models with four or more factors outperformed all three- and four-factor literature derived models. These models, while successful when fit to subscale scores in other studies, perform poorly at the item-level.

The winning model on AIC, BIC and SABIC was the novel 9-factor model. However, the structure of this model is quite different from Raine's 9 subscales (Table 4.2). This model showed good fit to the Validation set and to the 25 imputed full datasets, using a WLSMV estimator (Validation set: CFI = 0.931, TLI = 0.929, RMSEA = 0.031; Imputed datasets: CFI = 0.915; TLI = 0.913; RMSEA = 0.035). However, 3 of the inter-factor correlations exceeded 0.8 and one factor had fewer than 5 items, so the model did not meet validation criteria.

The novel 6-factor structure was the next best-fitting model on all indices compared to the next best novel model (the novel 7-factor model), though Raine's 9-factor model outperformed it on AIC and SABIC (Figure 4.5). However, despite its good performance in model comparison, Raine's model may have contained likely-redundant factors.

The novel 6-factor model fit well to the Validation set and to the 25 imputed datasets with a WLSMV estimator (Validation: CFI = 0.927, TLI = 0.924, RMSEA = 0.032; Imputed datasets: CFI = 0.914; TLI = 0.911; RMSEA = 0.036). Parameter estimates for the 6-factor model fit to 25 imputed datasets are given in Appendix B.

I interpreted the six factors as 'Asociality', 'Anomalous Experiences & Beliefs', 'Paranoid Ideation', 'Social Anxiety', 'Eccentricity' and 'Odd Speech'. Importantly, the structure of the 6-factor solution resolves the issue of highly overlapping domains identified in Raine's 9-factor model, as the factors that showed inter-factor correlations over 0.8 were mostly merged into single factors (Ideas of Reference & Suspiciousness; Unusual Perceptual Experiences & Magical Thinking; No Close Friends & Constricted Affect). Figure 4.6 is a river-plot showing how the original 9 SPQ subscales relate to the novel 6-factor solution.

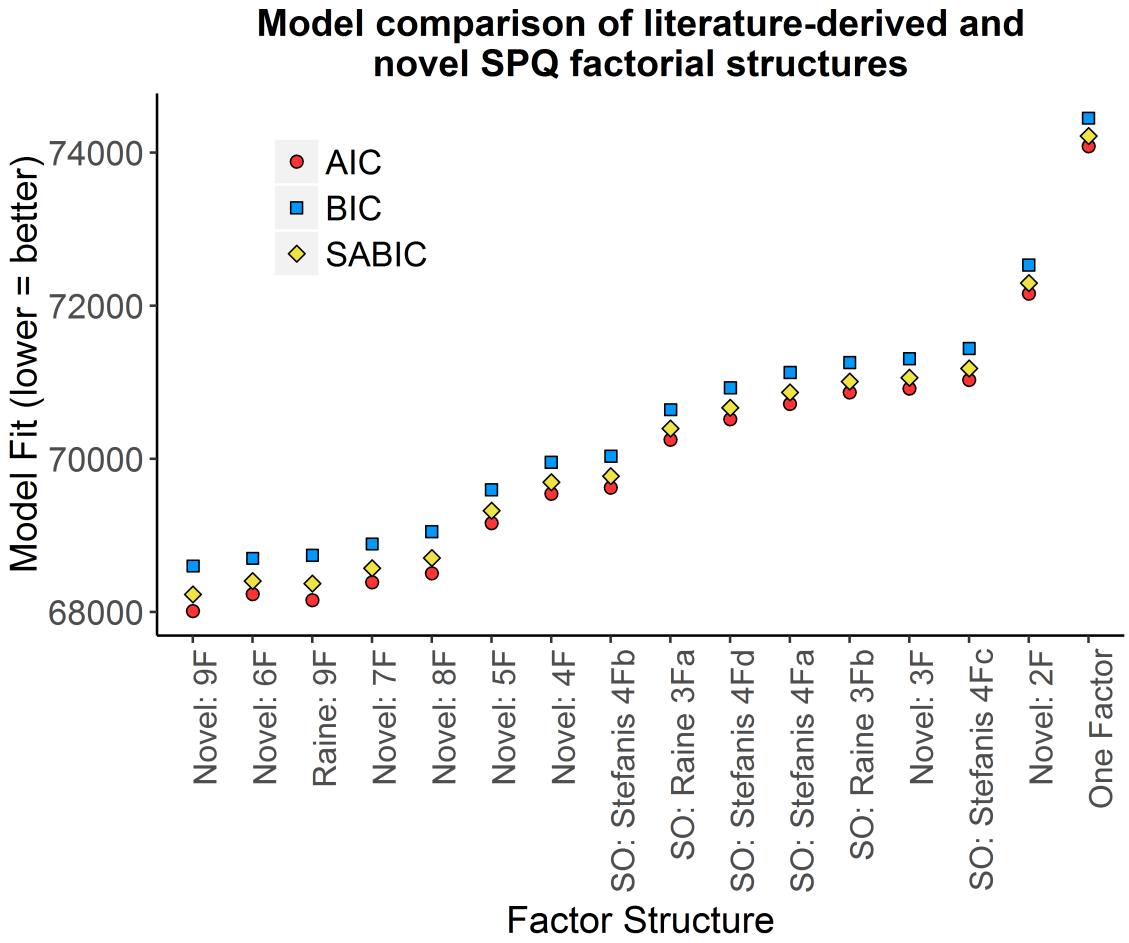


Figure 4.5: Model comparison of novel and literature-derived dimensional structures of the SPQ with three log-likelihood based indices (AIC, BIC, SABIC) that trade off model fit with model parsimony. Lower values indicate better performance.

Figure 4.6 Riverplot of relationship between the original 9-factors of the SPQ and the novel 6-factor model

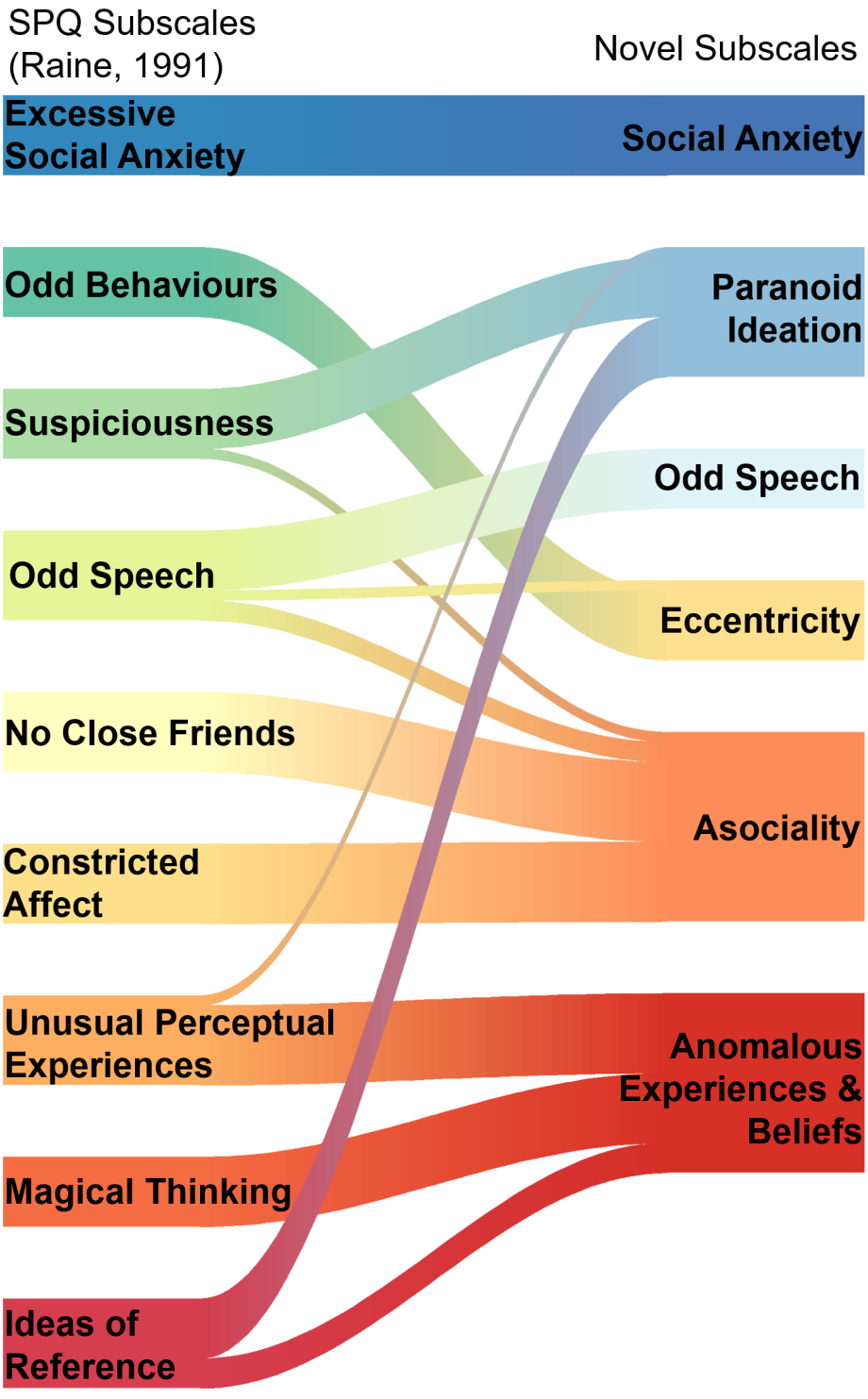


Figure 4.6: The structure of the 6-factor solution is recognisable in the 9-factor solution. Of the original 9 scales, those that showed very high inter-factor correlations have largely merged into larger factors in the 6-factor solution e.g. No Close Friends and Constricted Affect now form a larger Asociality construct, with some items from Odd Speech and Suspiciousness.

Table 4.5: Measurement properties of the 6-factor SPQ model. ω_T = 'Omega Total', the greatest upper bound on reliability. ω_H = 'Omega Hierarchical', the proportion of variance attributable to a single construct. α = Cronbach's (1951) 'coefficient alpha', reported for convention only. H = Loevinger's scaleability coefficient, an index of the strength of a Mokken scale. H > 0.3 = weak, H > 0.4 = moderate, H > 0.5 = strong. S.E.(H) = standard error of H. N IRF intersections = number of times IRFs intersect, indicating a failure of invariant item ordering. H_T = index of the strength of hierarchical ordering after items with intersecting IRFs were removed. $H_T > 0.3$ = weak, $H_T > 0.4$ = moderate. Higher H_T values show that sum scores are more likely to order participants by the latent trait.

Scale	ω_T	ω_H	α	H	S.E.(H)	N IRF intersections	H_T
Asociality	0.8	0.96	0.95	0.42	0.011	5	0.36
Anomalous Experiences & Beliefs	0.71	0.94	0.93	0.32	0.012	1	0.21
Paranoid Ideation	0.81	0.95	0.93	0.42	0.011	4	0.23
Eccentricity	0.83	0.95	0.93	0.55	0.012	2	0.46
Social Anxiety	0.89	0.93	0.91	0.52	0.011	3	0.44
Odd Speech	0.75	0.91	0.85	0.44	0.014	1	0.32

Measurement properties of the novel 6-factor solution

Table 4.5 shows the results of bifactor modelling with polychoric correlations (and coefficient alpha computed with Pearson correlations, for comparison to other literature). Every scale showed sufficiently high ω_H to compute sum scores and excellent internal consistency, indicated by $\omega_T > 0.9$.

Measurement precision across severity/intensity levels

Figure 4.7 shows the standard error of measurement across the range of the latent traits for all models, measured using 2PL pIRT models. Standard error curves are overlaid for factors from Raine's solution and the 6-factor solution that share at least 5 items.

Many of the factors show less precise measurement at the extremes of the latent trait, which is common, particularly in clinical or symptom-based scales. This is particularly true for the extreme low ends of some scales. While the curves for a number of scales are similar in both solutions, the 6-factor AEB and Aso factors have more precise measurement at both the extreme high and extreme low ends than Raine's scales. This improvement in precision is quite substantial for the AEB factor.

Figure 4.7 Measurement precision across the distribution of latent traits in the SPQ

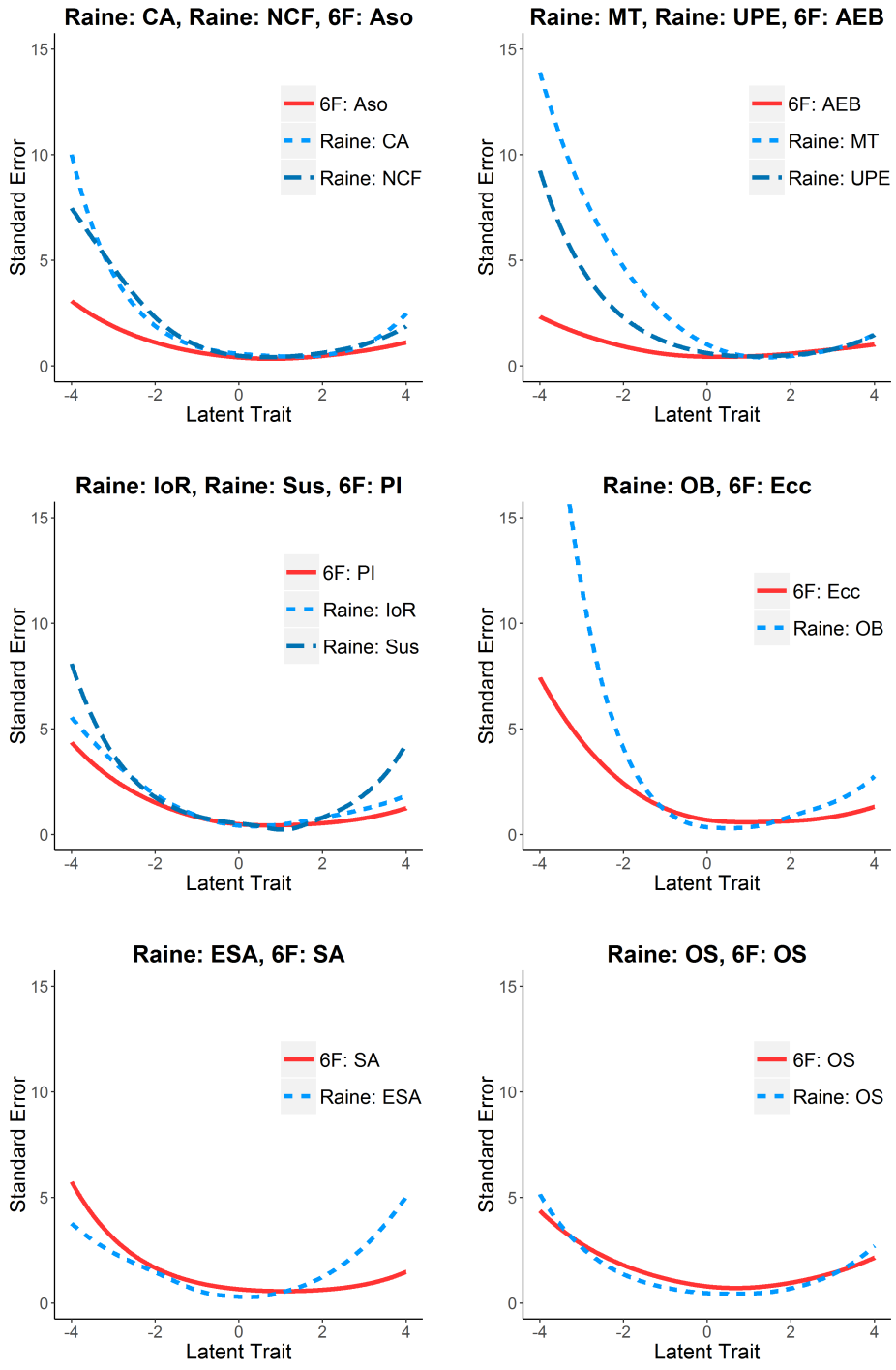


Figure 4.7: Measurement precision across the distribution of latent traits in the SPQ, calculated from parametric item response theory analyses. The novel 6-factor solutions are compared to scales from the original 9-factor model that share at least 5 items. The latent trait (x-axis) is scaled to 0-mean and unit variance. The novel factors improve measurement precision, relative to the original factors, indicated by lower standard error of measurement.

Appropriateness of sum scores to rank participants by severity/intensity

Results of nIRT analyses to investigate item hierarchies are also shown in Table 4.5. All of the scales formed at least a weak Mokken scale (H $>$ 0.3). All scales showed at least one significant intersection of IRFs, thus violating IIO. Subsets of items within 4 of the 6 novel scales contained hierarchies, evidenced by HT values greater than 0.3. However, none of the complete scales showed evidence of hierarchical ordering. This suggests that sum scores on all scales are likely to misorder some participants with respect to the trait in question.

Systematic biases caused by other characteristics

Table 4.6: Systematic biases with age/sex were investigated by increasingly constraining models fit to different groups to be equal and examining model fit, indexed by CFI. Aso, AEB and PI were strongly invariant over age and sex. Ecc, SA and OS were strongly invariance over age but only weakly invariant over sex, suggesting they may not be suitable to compare men and women.

	Invariance over age (14-17, 18-25) (CFI)					Invariance over sex (male/female) (CFI)				
Scale	Equiv. structures	Weak invariance	Change in fit (weak)	Strong invariance	Change in fit (strong)	Equiv. structures	Weak invariance	Change in fit (weak)	Strong invariance	Change in fit (strong)
Aso	0.957	0.965	0.008	0.963	-0.001	0.955	0.963	0.008	0.959	-0.004
AEB	0.914	0.927	0.013	0.921	-0.005	0.913	0.928	0.015	0.921	-0.007
PI	0.946	0.955	0.01	0.953	-0.003	0.946	0.955	0.009	0.951	-0.004
Ecc	0.992	0.994	0.002	0.994	0	0.992	0.994	0.002	0.982	-0.012
SA	0.997	0.998	0.001	0.997	-0.001	0.997	0.998	0.001	0.98	-0.018
OS	0.969	0.971	0.002	0.97	-0.001	0.969	0.972	0.002	0.958	-0.014

Table 4.7: Partial invariance of scales from the 6-factor SPQ model. For Ecc, SA and OS, strong invariance was achieved after allowing the thresholds for one item to differ across groups, suggesting that systematic biases due to sex may be small.

Scale	Item Number	Item	Fit with item unconstrained (CFI)	Change in fit from weak to strong invariance (CFI)
Ecc	5	Other people see me as slightly eccentric or odd	0.9856	-0.0083
SA	2	I sometimes avoid going to places where there will be many people because I will get anxious	0.9921	-0.0061
OS	7	People sometimes find it hard to understand what I am saying	0.9618	-0.0099

Results of measurement invariance testing are shown in Table 4.6. All factors in the novel solution showed invariant factor loadings with age (weak invariance) and invariant item thresholds (strong invariance), supporting that sum scores on these instruments can accurately compare adolescents and young adults.

All factors in the novel solution showed invariant factor loadings (weak invariance) with sex. Aso, AEB and PI also showed invariant thresholds (strong invariance). Ecc, SA and OS failed strong invariance, but partial invariance was achieved by allowing 1 item in each scale with the highest modification index to be equal across the groups (Table 4.7). These three scales may be less suitable for comparing men and women.

4.4.2 BSSI

Missing data: SPQ

Table 4.8: Missing data on the BSSI.The missing values were judged to meet missing-at-random (MAR) assumptions so were suitable for multiple imputation and estimation using full-information maximum-likelihood.

Reporting Guideline	Description
Number of missing values for variables of interest	966/1238 filled in BSSI (78.0% of baseline sample, 91.7% of time 3 sample). 917/966 had complete data (95.0% of filled in questionnaires, 74.1% of baseline sample). 42/48 partially complete questionnaires only had 1 item missing.
Possible reasons for missingness	Higher psychopathology, sociodemographic features (e.g. sex, low socioeconomic status)
Differences in key exposures and outcomes of interest in missing and observed data	Logistic regressions were used to predict having incomplete data on the BSSI from other variables (see "Variables used in imputation procedure" below). Numbers in brackets indicate OR and 95% CI. Incomplete data was predicted by: male sex (1.9, 1.47 - 2.46), low socioeconomic status (1.95, 1.38 - 2.75), years of maternal education (0.92, 0.87 - 0.98), lifetime PEs (1.67, 1.03 - 2.64), and childhood adversity (1.74, 1.31 - 2.30).
Assumptions about missing data?	Missing at random (MAR)
Imputation software	Predictive mean matching (PMM), Hmisc package, R for statistical computing

Table 4.8 – continued from previous page

N imputed datasets	25
Variables used in imputation procedure	Non-white ethnicity, SES, years of mother's education after age 16, family history of psychiatric disorder, lifetime, past-year and persistent psychotic experiences measured using the Psychotic-Like Symptoms Interview (Horwood et al., 2008) nonpsychotic disorders measured with the K-SADS-PL (Kaufman et al., 1997) (occurring before age 14, at age 14 and at age 17, age 14), childhood adversity between 0-14 measured with the CAMEEI (Dunn et al., 2011), age 17 item-level responses about depressive symptoms (MFQ) (Angold et al., 1995), age 14 and age 17 self-report anxiety symptoms (RCMAS) (Reynolds and Richmond, 1997), obsessive-compulsive symptoms (LOI) (Berg et al., 1986; Bamber et al., 2002), antisocial behaviours (BC) (Cousins et al., 2016), friendship quality (CFQ) (van Harmelen et al., 2016) family support (FAD) (Epstein and Baldwin, 1983) and age 17 self-report wellbeing (WEMWBS) (Tennant et al., 2007).
Approach to non-normal and categorical variables	PMM preserves the distribution of observed variables by borrowing real values from observed data that could plausibly be the missing value
Interactions	None included
Plausibility of observed and imputed values	Plot distributions of observed and imputed values
Plausibility of MAR assumption supported by variables included in imputation model?	Logistic regressions confirmed that missingness on individual BSSI items was predicted by one or more of the imputation variables.
Complete cases analyses	I also reported complete cases analyses
Sensitivity analyses	Not conducted, see Table 3.1 for justification.

The BSSI missing data was judged to be plausibly MAR (Table 4.8).

Endorsement of BSSI categories

The BSSI was answered on a 5-point frequency scale. Some of these categories were very rarely endorsed (Table 4.9). Rare endorsements make it difficult to estimate polychoric correlations, because it increases the number of combinations of response levels (cells in the bivariate table) with 0 participants, which must be corrected by adding a numeric constant (usually 0.5), which allows estimation but potentially adds noise to the data. A high number of response levels also makes latent variable models more computationally demanding, while potentially introducing unreliability as different people may not treat the distances between the levels equally. Sometimes, scales with large numbers of response levels are treated as continuous measurements. This is potentially inappropriate as the response intervals are not truly equally spaced. However, collapsing categories may lose valuable information that can separate more intense PEs from more attenuated ones.

I proceeded to test the factorial structure of the BSSI subscales by both treating the responses as continuous by using a robust ML (MLR) estimator, and treating data as categorical, using a WLSMV estimator, in the unmodified data, and a data sets in which 3 most extreme response categories were collapsed, to produce 3-point data. This ensured that no response categories were endorsed by less than 1% of the sample.

Redundant and Unrelated Items

When estimating polychoric correlation matrices from 5, 4 and 3 category data, 151, 47 and 1 cell(s) needed correcting for 0 responses of that pattern, respectively.

In all matrices, item 6, 'Do you often feel that other people have got it in for you?' and item 12, 'I often feel that others have it in for me' had correlations over 0.9. Item 6 had the lowest average inter-item correlation in all matrices and was removed. The other 19 items showed no redundantly high correlations and all items had at least 8 correlations over 0.3 in all matrices.

Literature-Derived Dimensional Structures

The three-factor model fit well to the 5-category data, both to complete cases data (N = 918, CFI = 0.920, TLI = 0.908, RMSEA = 0.052 (95% CI = 0.048 – 0.056)) and to partially complete data estimated using full-information maximum likelihood (N = 966, CFI = 0.920, TLI = 0.910, RMSEA = 0.052 (95% CI = 0.052 – 0.048)).

The model fit very well to the 5-category data with a WLSMV estimator, though with a large number of corrections for empty bivariate cells (N = 918, CFI = 0.977, TLI = 0.973, RMSEA = 0.063 (95% CI = 0.059 – 0.068)).

The WLSMV-estimated model also fit very well to the 3-category data, with only one correction for empty bivariate cells (N = 918, CFI = 0.974, TLI = 0.970, RMSEA = 0.059 (95% CI = 0.054 – 0.064)). The model also showed good fit to 25 imputed datasets (N = 1238, CFI = 0.915, TLI = 0.902, RMSEA = 0.040 (95% CI = 0.035 – 0.044)). The inter-factor correlations from the imputed model were: $r_{(AEB,\ SA)} = 0.32$, $r_{(AEB,\ PI)} = 0.57$, $r_{(SA,\ PI)} = 0.49$.

Table 4.9: Endorsement of response categories of the BSSI

		Not at all		Occasionally		Sometimes		Most of the time		Always		Sometimes or more	
Item Number	Item	N	%	N	%	N	%	N	%	N	%	N	%
1	I sometimes avoid going to places where there will be many people because I will get anxious.	647	70.56	157	17.12	111	12.1	43	4.69	8	0.87	162	17.66
2	Do you believe in telepathy (mind-reading)?	696	75.9	147	16.03	83	9.05	25	2.73	13	1.42	121	13.2
3	I am sure I am being talked about behind my back.	362	39.48	386	42.09	133	14.5	63	6.87	18	1.96	214	23.33
4	I get very nervous when I have to make polite conversation.	573	62.49	222	24.21	108	11.78	49	5.34	13	1.42	170	18.54
5	Have you had the sense that some person or force is around you, even though you cannot see anyone?	726	79.17	141	15.38	55	6	27	2.94	16	1.74	98	10.68
6	Do you often feel that other people have got it in for you?	654	71.32	222	24.21	56	6.11	24	2.62	7	0.76	87	9.49
7	I feel very uneasy talking to people I do not know well.	443	48.31	293	31.95	118	12.87	82	8.94	26	2.84	226	24.65
8	Have you noticed a common event or object that seemed to contain a special sign for you?	799	87.13	96	10.47	50	5.45	13	1.42	4	0.44	67	7.31
9	When you see people talking to each other, do you often wonder if they are talking about you?	561	61.18	268	29.23	86	9.38	34	3.71	11	1.2	131	14.29
10	I often hear a voice speaking my thoughts aloud.	823	89.75	73	7.96	34	3.71	16	1.74	14	1.53	64	6.98
11	Do you often feel nervous when you are in a group of unfamiliar people?	339	36.97	359	39.15	141	15.38	93	10.14	31	3.38	265	28.9
12	I often feel that others have it in for me.	724	78.95	159	17.34	50	5.45	23	2.51	4	0.44	77	8.4
13	Have you seen things invisible to other people?	878	95.75	57	6.22	17	1.85	6	0.65	1	0.11	24	2.61
14	I feel very uncomfortable in social situations involving unfamiliar people.	461	50.27	316	34.46	102	11.12	61	6.65	25	2.73	188	20.5
15	Do you sometimes feel that people are talking about you?	464	50.6	345	37.62	99	10.8	39	4.25	16	1.74	154	16.79
16	Can other people feel your feelings when they are not there?	845	92.15	82	8.94	20	2.18	6	0.65	2	0.22	28	3.05
17	I get anxious when meeting people for the first time.	335	36.53	393	42.86	109	11.89	89	9.71	36	3.93	234	25.53
18	Do you believe in clairvoyancy (psychic forces, fortune telling)?	706	76.99	147	16.03	62	6.76	25	2.73	22	2.4	109	11.89
19	Do you sometimes feel that other people are watching you?	606	66.09	241	26.28	88	9.6	16	1.74	13	1.42	117	12.76
20	Have you felt that you are communicating with another person telepathically (by mind-reading)?	900	98.15	43	4.69	14	1.53	7	0.76	1	0.11	22	2.4

The BSSI therefore has a well-fitting factorial structure with related factors that can probably be measured distinctly. I therefore did not use EFA to construct any novel factorial structures. Full parameter estimates from the full-information MLR-estimated model fit to 5-category data and the WLSMV-estimated model fit to 3-category imputed datasets are given in Appendix B.

Measurement properties of the BSSI dimensions

Table 4.10: Measurement properties of the BSSI scales. ω_T = 'Omega Total', the greatest upper bound on reliability. ω_H = 'Omega Hierarchical', the proportion of variance attributable to a single construct. α = Cronbach's (1951) 'coefficient alpha', reported for convention only.

	5 response categories			3 response categories		
Scale	ω_H	ω_T	α	ω_H	ω_T	α
SA	0.92	0.96	0.93	0.65	0.95	0.93
AEB	0.74	0.93	0.9	0.71	0.93	0.9
PI	0.88	0.93	0.9	0.88	0.93	0.9

Results of reliability testing using bifactor modelling are shown in Table 4.10. All scales of the BSSI showed a large proportion of variance explained by a general factor and good internal consistency.

Measurement precision across severity/intensity levels

Figure 4.8 shows information distributions for the BSSI scales. Notably, the 5-category model had better measurement precision at the more severe range of the trait. This suggested that the full 5-category solution captured meaningful variance that is lost by collapsing response levels, particularly in PI and SA. However, the gain in precision for AEB was low and the measurement precision of the 3-category data was still reasonable at high levels. There is therefore a trade-off between tractability and stability of analyses versus capturing variance at the most severe ranges of psychotic phenomena.

Figure 4.8 Measurement precision across the distribution of latent traits in the SPQ

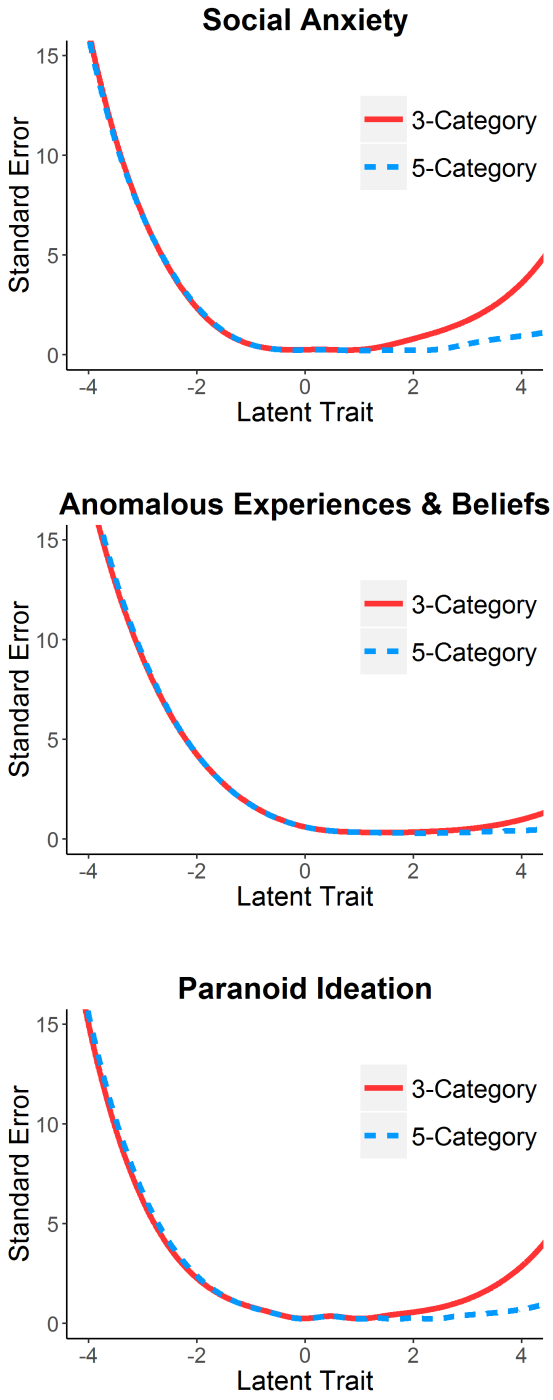


Figure 4.8: Measurement precision across the distribution of latent traits in the BSSI, calculated from parametric item response theory analyses. Collapsing responses from 5 to 3 categories loses some information at the extreme end of the distribution but improves the stability of latent variable modelling.

Appropriateness of sum scores to rank participants by severity/intensity

Table 4.11: Mokken scale properties of the scales of the 3-factor BSSI model. H = Loevinger's scaleability coefficient, an index of the strength of a Mokken scale. H > 0.3 = weak, H > 0.4 = moderate, H > 0.5 = strong. S.E.(H) = standard error of H. N IRF intersections = number of times IRFs intersect, indicating a failure of invariant item ordering. H_T = index of the strength of hierarchical ordering after items with intersecting IRFs were removed. H_T > 0.3 = weak, H_T > 0.4 = moderate. Higher H_T values show that sum scores are more likely to order participants by the latent trait.

	5 response categories				3 response categories			
Scale	H	S.E.(H)	N IRF intersections	H_T	H	S.E.(H)	N IRF intersections	H_T
SA	0.674	0.017	0	0.2	0.648	0.016	0	0.2
AEB	0.372	0.024	0	0.19	0.396	0.022	0	0.19
PI	0.622	0.021	0	0.3	0.607	0.019	1	0.3

Table 4.11

Results of Mokken scaling are shown in Table 4.11. All scales, particularly SA and PI, showed good Mokken scalability, supporting the use of sum scores, though there was little evidence of hierarchical item ordering; only the PI scale showed very weak hierarchical ordering. This suggests that sum scores may misorder some participants on the measured systems.

Systematic biases caused by other characteristics

Table 4.12: The BSSI scales showed strong invariance over sex, indicating no systematic bias across male and female adolescents.

	Invariance over sex (male/female) (CFI)				
Scale	Equiv. structures	Weak invariance	Change in fit (weak)	Strong invariance	Change in fit (strong)
SA	0.998	0.997	-0.001	0.997	0
AEB	0.974	0.969	-0.005	0.96	-0.009
PI	0.996	0.996	0	0.995	0

Table 4.12

Results of measurement invariance testing over sex are shown in Table 4.12. The models fit to the 5-category data did not converge for the AEB scale due to very low numbers of item endorsements. I therefore reported results from 3-category data only. All scales showed weak

and strong measurement invariance, supporting the use of sum scores to compare males and females on this instrument.

4.5 Summary

Thorough analysis of the measurement properties of two instruments measuring psychotic phenomena, the Schizotypal Personality Questionnaire (SPQ) and the Brief Schizotypal Symptoms Inventory (BSSI), revealed strengths and weaknesses of each instrument.

4.5.1 SPQ

The dominant three-factor and four-factor structures of the SPQ in the literature are likely to be artefacts of the subscale constructions. Some subscales of the SPQ are unlikely to be measuring distinct constructs, particularly: Ideas of Reference (IoR) and Suspiciousness (Sus), Constricted Affect (CA) and No Close Friends (NCF), and Magical Thinking (MT) and Unusual Perceptual Experiences (UPE). These similarities may underlie why there are inconsistent findings regarding the factorial structure of the SPQ. In Raine's 3-factor model IoR, Sus, MT and UPE all load on to a 'Cognitive-Perceptual' factor. In the major challenger to this structure, the four-factor model of Stefanis et al. (2004), IoR and Sus load on to a specific Paranoia factor. Fluctuations and variable measurement error across samples may lead to the correlations between IoR and Sus items and between MT and UPE items being attenuated or exaggerated, which may lead to better or worse fit for a single latent factor constructed from all of them.

The factorial structure I identified is very similar to that of Watson et al. (2008), in that closely related pairs of SPQ subscales largely merged into larger scales. In that study, a 5-factor model won overall but a 6-factor model also fit the data well, with the difference being the division of an 'Eccentricity/Oddity' factor into odd speech and odd behaviour, as was evident in the 6-factor model I identified. Watson interpreted their findings in terms of the dimensions of schizotypal personality disorder. However, the high correlations between SPQ scales and the Chapman schizotypy scales (Wuthrich and Bates, 2006), which are conceptually closer to Meehl's (Meehl, 1962) model of schizotypy, and the fact that these results were obtained in the general population, supports a broader interpretation. To what extent the factors identified are specifically associated with positive psychotic experiences is a question of further research. For example, asociality (or social anhedonia, as Watson et al. (2008) described their factor comprising No Close Friends and Constricted Affect), is far from limited to those with psychotic experiences and social difficulties feature in most, if not all, psychiatric disorders. Similar phenomena, like social difficulties and social anxiety, are measured across research into different psychiatric domains, and the tendency for 'working in silos' means specificity and 'transdiagnosticity' have rarely been investigated. In the general population, this is likely to be particularly important, as the early stages of psychopathology may present as general and nonspecific symptoms (Stochl et al., 2015), before crystallising into more recognisable disorders at greater severity (McGorry et al., 2014).

Practically, these results provide a set of 6 interpretable scales of the SPQ that are largely unidimensional, have high internal consistency, have reasonable measurement precision over the full

range of the systems being measured (particularly the Asociality (Aso), Anomalous Experiences & Beliefs (AEB) and Paranoid Ideation (PI) scales), can be used as sum scores, are equally able to measure adolescents and young adults and, for Aso, AEB and PI, are also strongly invariant over sex. These results support little advantage in using the 9 subscales of the SPQ and strongly question the validity of the three-factor and four-factor models that are often considered to be the basic structure of schizotypy (Kwapil and Barrantes-Vidal, 2015).

4.5.2 BSSI

Beyond a single redundant pair of items, the BSSI demonstrated few psychometric weaknesses. The three-factor model, comprising Social Anxiety, Anomalous Experiences & Beliefs and Paranoid Ideation fit the data well, whether the original 5 response categories were used or the severe categories were collapsed due to low endorsement. When used as a 5-category instrument, it provides high measurement precision even up to severe levels of the systems measured and can be used as a sum score. The BSSI scales are largely unidimensional, have high internal consistency and are strongly invariant over sex.

However, large numbers of rarely endorsed categories can cause some methods, like latent variable modelling, to fail or be unreliable. I therefore recommend that sum scores on the BSSI be calculated from the 5-category data, but latent variable modelling or similar analyses where rarely endorsed levels are problematic should consider collapsing response categories. The information loss from collapsing categories was minimal for Anomalous Experiences and Beliefs, though slightly more for Social Anxiety and Paranoid Ideation.

4.5.3 General summary

Both instruments showed, with some revision, to give adequate measurements of psychotic phenomena. However, the extents to which these phenomena are related to definite psychotic experiences (PEs) and to more general distress, depressive symptoms or anxious symptoms remains unclear. This work supports that both instruments can be taken forward in revised forms for future empirical work.

4.5.4 Strengths & limitations

This study was strengthened by use of large, representative or near-representative cohorts of young people, rigorous psychometric assessment, generation and validation of models in a split sample (for the SPQ) and near-replication of model structures in the literature. A major limitation, shared with the theory of schizotypy generally, is the lack of external validation that the associations between so-called 'schizotypal' traits are more associated with one another than traits that are not schizotypal, like depressive symptoms, general anxiety or obsessive symptoms.

The results of this study will be discussed in greater detail at the end of the next chapter in a broader consideration of the measurement of PEs.

Chapter 5

Self-report and interview instruments measure overlapping but partially-distinct severity ranges of the same psychotic phenomena in adolescents

Abstract

Psychotic experiences (PEs) can be measured by self-report instruments or interview instruments, where the veracity of the PEs is externally assessed. These instruments tend to be developed and applied in different fields; self-report instruments through schizotypy and individual differences frameworks and interview instruments through clinically-oriented psychosis-risk research. It is not known whether self-report and interview instruments measure the same underlying phenomena and whether they measure PEs of the same or different severity/intensity. In this chapter, I used data from a representative cohort of 1054 17-year-olds to compare self-report and interview measurements of PEs. 'Verified' (interview-assessed) PEs had a lifetime prevalence of 12.6%. Combining two dimensions of self-report PEs in the past two weeks (AEB: anomalous experiences and beliefs; PI: Paranoid Ideation) improved criterion validity of predicting lifetime verified PEs but some people with past verified PEs had no current self-report PEs. Comparison of latent variable modelling showed that a common underlying factor underlies both self-report AEB and PI and verified PEs, explaining 77.5% of the total variance. In comparison, two correlated factors best explain self-report social anxiety and verified PEs. Item response theory analysis showed that interview items measured PEs of high severity, but that self-report items could measure PEs of similar severity and also measured PEs of far lower severity. These results indicate that self-report and interview instruments measure partly-overlapping severity ranges of a common underlying distribution and support the validity of self-report measurements.

5.1 Research Questions

- Do instruments designed to measure different theoretical conceptualisations of PEs measure the same underlying phenomena in young people?
- If so, do they measure the same or distinct severity ranges of PEs?

5.2 Introduction

PEs are measured by a large number of different instruments, often designed to measure subtly different theoretical conceptualisations of them. While the details of these theories and the precise measurements vary across instruments, medium to high correlations are often observed between them (Peters et al., 2004; Kwapil et al., 2008; Compton et al., 2009; Kline et al., 2012; Cicero et al., 2014), raising the possibility that they may largely be measuring the same thing.

A crucial difference between families of instruments is between 'verified' instruments that use an assessor's judgment and/or a set of criteria to verify whether a reported phenomenon should be classified as a psychotic or psychotic-like experience, and 'self-report' instruments that accept a person's response without verification. The former are predominantly interview instruments, while the latter are predominantly questionnaires. Differences in measurement type, study designs and study cohorts account for half of the heterogeneity in rates of psychotic phenomena in the general population (Linscott and Os, 2010). In particular, self-report assessment is associated with higher rates of psychotic phenomena than verified assessment.

Verified and self-report instruments might be considered as arising from different traditions; verified instruments are descended from clinical practise while self-report instruments are more closely related to personality research. These traditions take different approaches to ensure the quality of their measurements. Verified instruments rely on more detailed questioning, expertise of another person or group of people and a set of criteria that allow standardization of diverse phenomena. Given appropriate instrument properties and implementation, one could argue that verified instruments should measure PEs with negligible measurement error.

Many self-report instruments rely on using a set of items, like statements or questions, and model the covariance between them as if it were explained by an unobservable or 'latent' variable, such as 'cognitive-perceptual schizotypy' (Raine et al., 1994). This latent variable explains some of the variance in the measured responses, though some residual variance is attributed to measurement error. It is accepted (and explicitly modelled, in latent variable modelling) that every item is measured with error. This error often makes single items unreliable. Item responses on self-report instruments are usually summed for an instrument/scale, generating a total score that provides a continuous estimate of the latent variable. Sometimes, self-report items are used in isolation, particularly in screening instruments. Here, the aim is often to establish a quick and reliable way to predict or rule out psychotic phenomena that could be confirmed or disconfirmed with a verified instrument. There is evidence that self-report psychotic phenomena predict verified psychotic phenomena, though a large number of self-report experiences fail to meet verification criteria (estimates of proportion of non-verification include 7% (van Os et al., 2001), 61% (Kelleher et

al., 2011) and 64% (van Nierop et al., 2012).

However, accumulating evidence shows that self-report PEs that fail to meet verification criteria are still associated with increased risk of psychotic disorder (Bak et al., 2003.; Poulton et al., 2000), as well as psychopathology and exposure to risk factors (van Nierop et al., 2012). This suggests that verification may discard valuable information in some cases and the border between 'psychotic' and 'non-psychotic' may be more nuanced than the boundary imposed by interview measurements.

Different instrument types may therefore be measuring common psychotic phenomena, but measuring different severity ranges with varying precision. In this chapter, I set out to test whether a self-report questionnaire of state psychotic phenomena and a verified interview instrument of lifetime PEs measured the same thing.

In the first set of analyses, I investigated the characteristics of PEs in this cohort as measured by a verified interview instrument. In the second set, I tested whether and to what extent self-report psychotic phenomena and verified PEs measure a common factor using latent variable modelling. As a control, I tested whether a single factor also explained combined interview items on PEs and self-report measurements of social anxiety. Then, were verified and self-report items shown to measure a common psychosis factor, I tested whether they measured overlapping or distinct severity ranges.

I predicted that a single underlying factor would explain most of the variance in interview and self-report PE items but that two correlated factors would explain combined PE and social anxiety items. I predicted interview items would measure a more severe range of PEs that self-report items would not measure well, which could produce 'ceiling effects' when self-report items are used alone. Similarly, I predicted interview items would not measure variance in less severe psychosis-proneness, which could be valuable in some studies as a predictor of future health and when studying underlying cognitive/brain mechanisms of psychosis.

5.3 Methods

5.3.1 Instruments

The Brief Schizotypal Symptoms Inventory

Self-report PEs were measured using the Brief Schizotypal Symptoms Inventory (Hodgekins et al., 2012) (BSSI). For detailed information and analysis of the measurement properties of the BSSI, see Chapter 1. The Brief Schizotypal Symptoms Inventory (BSSI) is a 20-item self-report instrument measuring psychotic phenomena in the last two weeks. It measures three domains: Anomalous Experiences and Beliefs (AEB), comprising perceptual abnormalities and magical thinking (8 items); Paranoid Ideation (PI), comprising suspiciousness and ideas of reference (6 items, of which one is redundant); and Social Anxiety (SA, 8 items). One item from PI is redundant with another and was removed.

Questions were structured as a set of statements or questions. Participants indicated how often

that statement applied to them in the last two weeks on a 5-point scale ('Not at all', 'Occasionally', 'Sometimes', 'Often' and 'All the time'. SSI scales are likely to be unidimensional (ω_H: SA = 0.65, AEB = 0.71, PI = 0.88) and have high internal consistency (ω_T: SA = 0.95, AEB = 0.93, PI = 0.93) (Revelle and Zinbarg, 2009).

Due to low endorsement of some categories, in analyses using latent variable modelling, responses were collapsed into a 3-point scale ('Not at all', 'Occasionally', 'Sometimes/Often/All the time'). Collapsing these high-severity responses loses some measurement precision at the more severe ranges of the traits, more so for PI and SA than AEB, but is necessary for model convergence.

Sum scores calculated form 5-category data may preserve this information, so in all analyses other than latent variable modelling, sum scores were calculated from the original response categories.

The Psychotic-Like Symptoms Interview

A modified version of the Psychotic-Like Symptoms Interview (Horwood et al., 2008) (PLIKSi), was administered to participants in schools, mostly during free periods. Due to time constraints, the initial opening questions, designed to put participants at ease, were omitted. In addition to the 12 core PEs, it measured 5 additional types. The types of PEs measured were auditory hallucinations, visual hallucinations, hallucinations not-otherwise-specified, derealisation, depersonalisation, bodily distortion, body dysmorphia, delusions of being spied on, delusions of persecution, delusions of thoughts being read, delusions of reference, delusions of control, delusions of grandiosity, delusions not-otherwise-specified, thought broadcasting, thought insertion and thought withdrawal.

Each PE type occurring over the lifetime was initially probed using a base question, then probed further to verify whether the experience was a definite PE, a possible PE or not a PE. Possible PEs were discussed at consensus meetings with a consultant psychiatrist (P.B. Jones) in an attempt to assign them to either definite or no PEs.

When participants endorsed a base question, further information was then acquired on the age of onset of the PE, its persistence (single experience, weeks, months, or a year or more), whether they were always or sometimes attributable to other factors like sleep, illness or substance use and whether they occurred in the past year.

In the first part of this chapter, I report the results of PLIKSi assessments in this population. For the remaining sets of analyses, I grouped lifetime PEs into hallucinations (visual, auditory, not-otherwise-specified), delusions (persecution, being spied on, mind-reading, control, reference, grandiosity and other unspecified delusions) and 'anomalous experiences' (thought broadcasting, thought insertion, thought withdrawal, body dysmorphia, bodily distortion, depersonalisation, derealisation) and also used composite variables of any lifetime PEs and any PEs definitely occurring in the past year.

5.3.2 Data

Data came from the ROOTS cohort (Lewis et al., 2016). All data were collected at the third time point, when participants were aged 17. For further information on ROOTS, see Methodology.

5.3.3 Analysis Set 1: PEs in the ROOTS cohort

I calculated the prevalence and persistence of lifetime and past-year PEs in any modality and for specific hallucinations, delusions or anomalous experiences. I calculated the occurrence of multiple PEs, persistence of PEs across modalities, the age of onset of PEs and the relationships between age of onset and persistence.

5.3.4 Analysis Set 2: Analysis of underlying latent variables

Latent variable model comparison

I used latent variable modelling to test to what extent the different instruments are measuring a common psychosis factor. I performed model comparison of four latent variable structures (Figure 5.1) fit to the data from combined instruments, firstly for PLIKSi, AEB and PI items and secondly, as a control, for PLIKSI and SA items.

The models structures are:

- A unidimensional model
- A correlated-factors model (one factor per instrument/subscale)
- An uncorrelated-factors model (one factor per instrument/subscale)
- A bifactor model (one general factor explaining some variance in all items and specific factors for residual variance in instruments/subscales)

I fit these models using a robust full-information Maximum Likelihood estimator (MLR), estimating partially incomplete missing data patterns using maximum likelihood. I compared models on log-likelihood-based fit indices that trade-off model fit with model parsimony (AIC, BIC and SABIC). The model with the lowest values was the winner. If a unidimensional or bifactor model fit the data best, I re-estimated that model with a robust weighted-least-squares (WLSMV) estimator. In the previous chapter, I fit WLSMV models to imputed datasets to account for missing data. In this chapter, I fit WLSMV-estimated models only to complete-cases data for three reasons. Firstly, analyses with many imputed datasets are computationally demanding. Secondly, the results of complete cases and imputed analyses in Chapter 4 were very similar, suggesting that bias due to using only complete-cases may be low. Finally, the item response theory methods I used to estimate item information distributions were only supported for complete-cases data in R at time of analysis.

Figure 5.1: Family of model structures compared

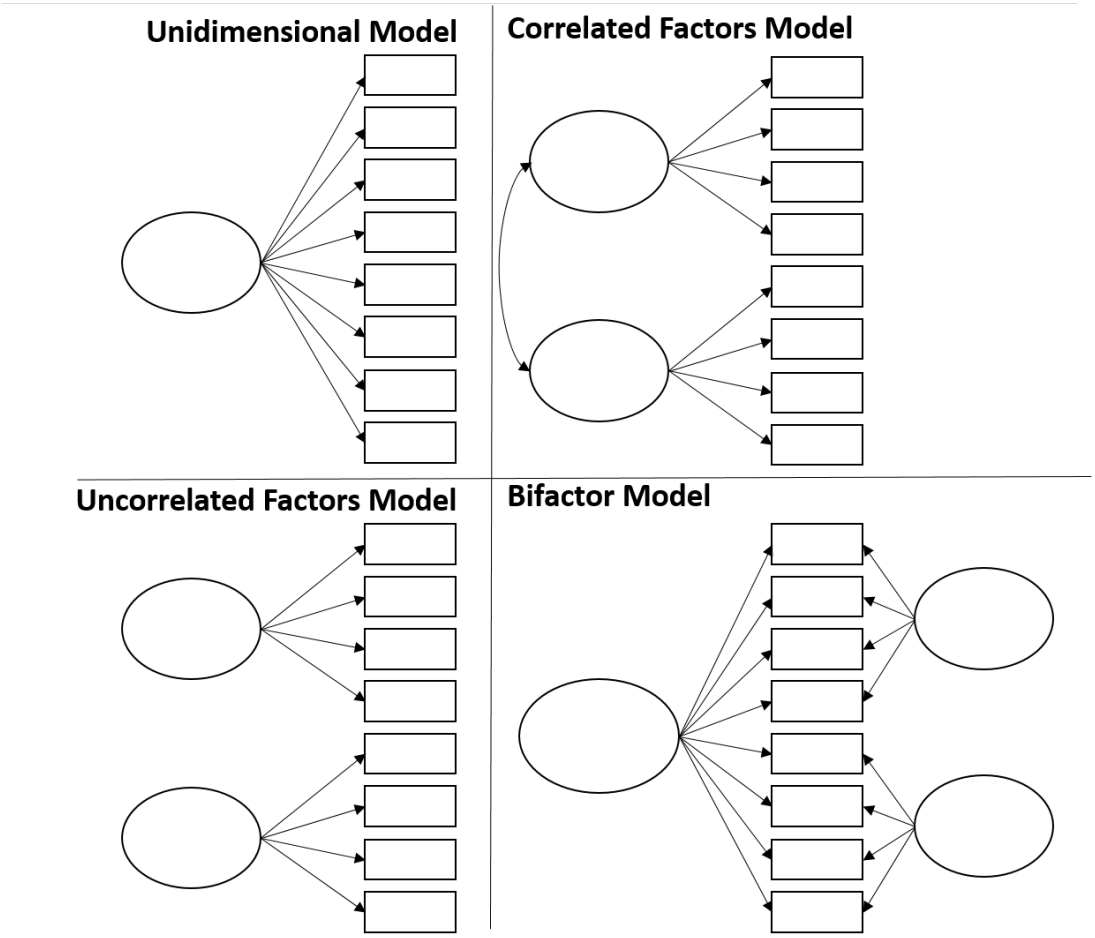


Figure 5.1: Diagrams of latent variable model structures. To investigate whether self-report and interview instruments measured the same underlying PEs or distinct constructs, I compared a model with a single factor, two uncorrelated factors, two correlated factors or a bifactor model with a general factor explaining common variance and specific factors explaining residual instrument-specific variance.

To what extent do self-report and verified items measure a common psychosis factor?

Even were a bifactor model to outperform the other models, it was still possible that the general factor would not explain a large proportion of the variance. I calculated ω_{H}, the proportion of variance explained by the general factor. I also approximated ω_{T}, the variance in the test that is attributable to all meaningful (non-noise) sources of variance, and variance explained by each specific factor and variance attributable to noise/error. For further details on ω statistics, see Chapter 4.

For factor models estimated from ordered categorical items, calculating ω is non-trivial due to the complexity introduced by having item thresholds summarising continuous distributions. I calculated ω_{H}, a specific type of ω coefficient, for the general factor. This provided a conservative but more appropriate approximation of the variance attributable to a single factor. The concept is identical to that of ω as described in Chapter 4, but the decimator changes to give a more conservative estimate (using the observed variance-covariance matrix, instead of the model-implied variance-covariance matrix, which gives a more conservative estimate because the model assumes perfect fit). I provided 95% bootstrap confidence intervals for ω_{H}.

Measuring different levels of psychosis severity (I): item threshold comparison

The WLSMV-estimated model allowed the calculation of item thresholds, which are the values of severity of the latent variable at which different categorical responses are emitted e.g. 'Hallucinations present' versus 'Hallucinations absent'.

I compared thresholds for interview items and for each level of the self-report items. If the locations of the thresholds for interview items exceeded all thresholds for self-report items, it would have suggested they measure a more severe range of the latent trait that is not measured by self-report items. Similarly, if self-report items had lower thresholds than all interview items, it would have suggested they more extensively measured lower-severity psychosis.

Measuring different levels of psychosis severity (II): test information distributions

If a unidimensional or bifactor model fit the data best, I planned to fit two-parameter logistic (2PL) item response theory (IRT) models using an Expectation-Maximization (EM) algorithm. This allowed the estimation of 'information' contributed per item. The standard error of measurement is inversely proportional to the square root of information at a given severity, so I could quantify measurement precision across any severity range. Information is additive, so total information distribution for self-report and verified items can be calculated and compared. If an information distribution spans a severity range not covered by another, it shows that there are differences in the severities of psychosis-proneness that the instruments are capable of measuring.

IRT models traditionally assume a normal distribution of the latent trait. This is unlikely to be the case for psychosis-proneness, given evidence of skewed trait distributions. Therefore, I estimated IRT solutions using both the assumption of a Gaussian trait distribution and using an

'empirical histogram' method, that constructs priors on the distribution of the latent trait based on item scores.

5.3.5 Implementation

All analyses were performed in R (R Core Team, 2016), augmented by packages *lavaan* (Rosseel, 2012), *semTools* (semTools Contributors, 2016), *mirt* (Chalmers, 2012) and *psych* (Revelle, 2014).

5.3.6 Supplementary analysis: Concurrent associations between self-report PEs and depressive symptoms

Interview-verified PEs can be modelled as a marker of severe common mental distress. In addition to investigating whether a common factor explained interview-verified and self-report PEs, I tested the concurrent validity of self-report PEs by testing whether they also index severe common mental distress in a replication of the study by Stochl et al. (2013), in both NSPN and ROOTS. For full details, see Appendix C.

5.4 Results

Of the 1238 participants who entered the study, 1074 took part at the third time point. 1056 participants completed the PLIKSi. 966 participants completed the BSSI.For discussion of missing data on the BSSI and investigations to support missing-at-random (MAR) assumptions, see Chapter 4.

914 participants had complete data on all BSSI scales and the PLIKSi.

Table 5.1: Prevalence and persistence of interview-verified PEs in ROOTS

Variable	N	%
Any PEs (Including Attributions)	156	14.8
Any PEs	133	12.6
Any Definite PEs In Past Year	84	8
Definite/Possible PEs In Past Year	94	8.9
Any Transient PEs	26	2.5
Any PEs Persisting For Weeks/Months	32	3
Any PEs Persisting For At Least 1 year	68	6.4
Any PEs Persisting For Years, Including Definite Last Year	52	4.9
Any PEs Persisting For Years, Including Definite/Possible Last Year	57	5.4
Single PE Type	88	8.3
Multiple PE Types	45	4.3
Grouped Hallucinations	74	7
Grouped Delusions	68	6.4
Grouped Anomalous Experiences	28	2.7

Table 5.1: For Ecc, SA and OS, strong invariance was achieved after allowing the thresholds for one item to differ across groups, suggesting that systematic biases due to sex may be small.

5.4.1 Analysis Set 1: PEs in the ROOTS Cohort

Prevalence of lifetime and past-year PEs in adolescents

Table 5.2: Endorsement of specific PEs in ROOTS

	None		Possible		Definite	
Psychotic Experience	N	%	N	%	N	%
Auditory Hallucinations	1022	96.8	2	0.2	32	3
Visual Hallucinations	1007	95.4	2	0.2	46	4.4
Derealisation	1045	99	0	0	10	0.9
Depersonalisation	1043	98.8	1	0.1	12	1.1
Bodily Distortion	1051	99.5	0	0	5	0.5
Body Dysmorphia	1056	100	0	0	0	0
Perceptual Anomalies	1041	98.6	0	0	15	1.4
Delusions Of Being Spied On	1007	95.4	0	0	49	4.6
Delusions Of Persecution	1052	99.6	1	0.1	2	0.2
Delusions of Thoughts Being Read	1048	99.2	0	0	7	0.7
Delusions Of Reference	1045	99	2	0.2	8	0.8
Delusions Of Control	1052	99.6	0	0	3	0.3
Delusions Of Grandiosity	1048	99.2	0	0	7	0.7
Other Delusions	1053	99.7	0	0	2	0.2
Thought Broadcasting	1051	99.5	1	0.1	3	0.3
Thought Insertion	1053	99.7	0	0	2	0.2
Thought Withdrawal	1054	99.8	0	0	1	0.1

1056 adolescents completed the PLIKSi at age 17 (see Table 5.1). Of these, 156 (14.8%) had one or more lifetime PEs. 6 (0.6%) further adolescents had possible lifetime PEs only. PEs were always attributable to sleep, illness or drugs in 23 participants, leaving 133 participants (12.6%) with definite, unattributable PEs.

236 definite individual lifetime PEs and 9 possible individual lifetime PEs were endorsed overall. Due to the low number of possible PEs, I included only definite PEs in further analyses. Of the 236 PEs, 32 always had an attribution to sleep, illness or drugs (Sleep: 14, Drugs: 12, Illness: 6), leaving 204 unattributable definite lifetime PEs.

84 adolescents (8.0%) definitely experienced a combined total of 117 individual PEs in the past year. Including definite lifetime PEs that possibly occurred in the past year means 94 adolescents experienced a combined total of 133 definite lifetime PEs in the past year.

Persistence of lifetime and past-year PEs

Most lifetime PEs were ones that persisted for at least a year. Data on PE persistence over the lifetime was available for 169 of the 204 definite, unattributable lifetime PEs. 28 (16.6%) were single experiences, 43 (25.4%) had persisted for weeks or months and 98 (58.0%) had persisted for at least one year. Of the full sample, 26 (2.5%) experienced one or more transient, single-occurrence PEs, 32 (3%) had one or more PEs that lasted for weeks/months and 68 (6.4%) had one or more PEs that persisted for at least a year.

Similarly, most PEs that occurred in the last year at age 17 were ones that had occurred for at least one year, though information was not available on how frequent they had been over that period. Data on the persistence was available for 107 of the 117 lifetime PEs definitely occurring in the past year. 10 (9.3%) were single occurrences, 27 (25.2%) lasted for weeks/months and 70 (65.4%) had persisted for at least one year. Data on the persistence was available for 118 of the 133 lifetime PEs definitely or possibly occurring in the past year. 13 (11.0%) were single occurrences, 28 (23.7%) lasted for weeks/months and 77 (65.3%) had persisted for at least one year.

Modalities of PEs

See Table 5.1 for prevalence of definite PEs grouped into modalities and Table 5.2 for possible and definite occurrences of individual types of PEs.

Lifetime hallucinations (N individual PEs = 93, 45.6% of lifetime PEs) and lifetime delusions (N individual PEs = 78, 38.2% of lifetime PEs) were more common than lifetime anomalous experiences (N individual PEs = 33, 16.2% of lifetime PEs).

Similarly, past-year hallucinations (N individual PEs = 47, 40.2% of past-year PEs) and delusions (N individual PEs = 51, 43.6% of past-year PEs) were more common than anomalous experiences (N individual PEs = 19, 16.2% of past-year PEs).

Occurrence of multiple PEs

Table 5.3: Prevalence of multiple co-occurring PEs.

Number of PEs	N	% of full sample	% of adolescents with PEs
0	920	87.1	NA
1	88	8.3	66.2
2	27	2.6	20.3
3	12	1.1	9
4	4	0.4	3
5	2	0.2	1.5

Some adolescents had multiple individual (ungrouped) PEs (see Table 5.3). Two-thirds of adolescents (66.2%) who experienced PEs experienced a single type, though some experienced up to 5 individual PEs (ungrouped).

PEs in one modality-group increased the likelihood of PEs in other modality-groups. A series of univariate logistic regressions indicated that the odds of hallucinations increased with experience of delusions (OR = 7.70, 95% CI = 4.08 – 14.11) and with anomalous experiences (OR = 6.41, 2.41 - 15.35). Odds of delusions increased with hallucinations (OR = 7.70, 4.08 – 14.11) and with anomalous experiences (OR = 17.38, 7.47 – 40.21). Odds ratios and confidence intervals for regressions with anomalous experiences as the outcome variable are equal to those in which it is a predictor variable for delusions/hallucinations.

Persistence of lifetime PEs across modalities

PEs grouped into different modalities had different patterns of durations. In all modalities, most PEs occurred for at least one year (Hallucinations: 27.8% = Single Experience, 17.7% = Weeks/Months, 54.4% = > 1 year; Delusions: 5.1% = Single Experience, 28.8% = Weeks/Months, 66.1% = > 1 year; Anomalous Experiences: 9.7% = Single Experience, 38.7% = Weeks/Months, 51.6% = > 1 year). Most single-experience PEs were hallucinations (78.6% of all single experiences).

Age of onset of PEs

Age of onset of PEs was available for 178 of the 204 definite lifetime PEs. Onsets were distributed across development, though were more common in adolescence (Figure 5.2). When PEs were reported to occur over the entire lifetime or since birth, an onset of 0 was recorded. Due to the probable unreliability of retrospective reporting from very early life, nonparametric statistics were used to avoid influence of extreme values and distributional assumptions.

Figure 5.2: Age of onset of PEs

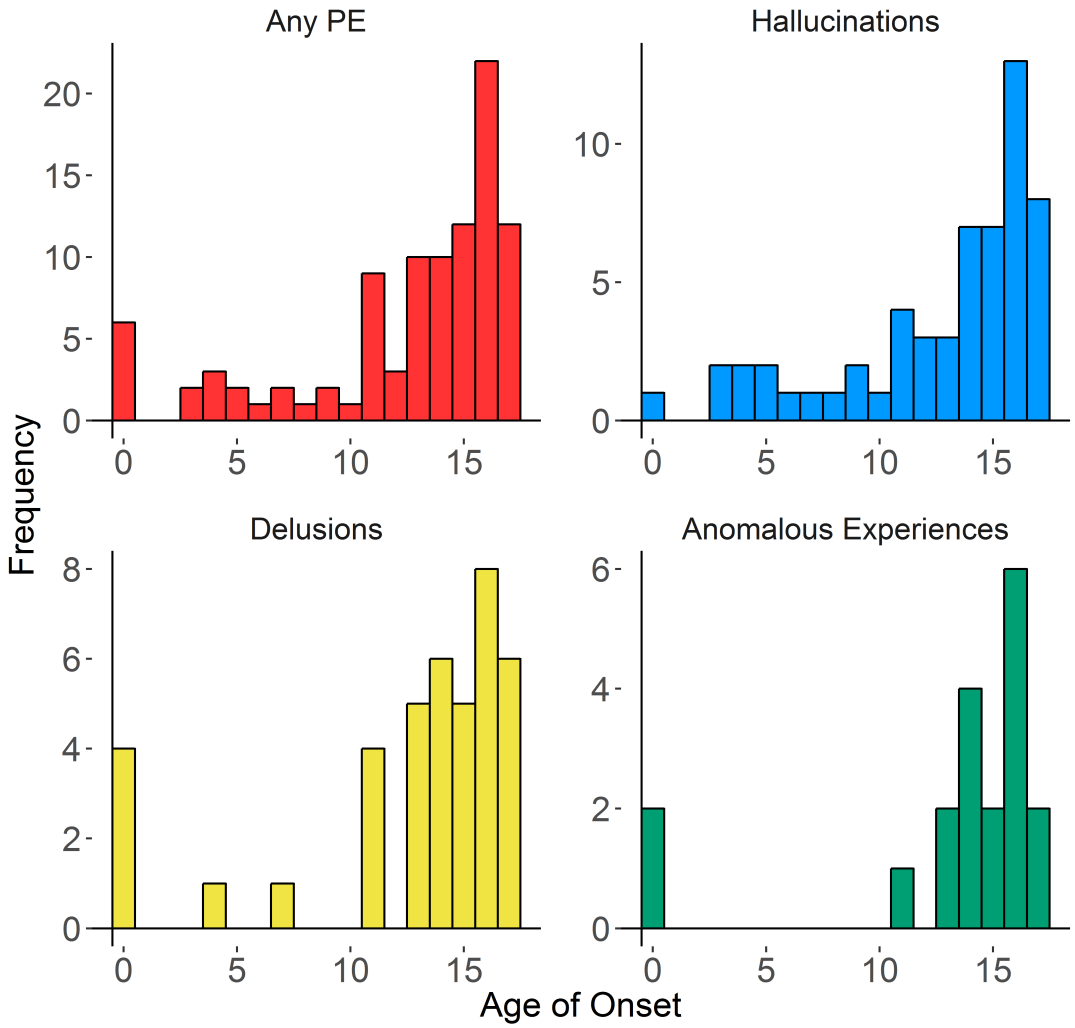


Figure 5.2: Age of onset of any PEs and PEs grouped into hallucinations, delusions and anomalous experiences. The majority of PEs had their onsets in adolescence, though some PEs occurred for as long as the participant could remember, indicated by an onset of 0 years.

Table 5.4: Results of comparison of different model structures fit to combined interview and self-report PEs

Model	AIC	BIC	SABIC
Unidimensional	18353.31	18591.68	18439.23
Three Correlated Factors	17438.30	17691.57	17529.59
Three Uncorrelated Factors	17751.22	17989.59	17837.13
Bifactor A	17081.01	17398.83	17195.56
Bifactor B	17239.46	17557.28	17354.01

Table 5.4: Results of model comparison of competing structures fit to self-report and interview PEs data using fit indices that trade-off model fit with model parsimony. Lower values indicate better fit. The winning model was Bifactor B with a specific factor for each instrument, followed by Bifactor A with a specific factor for PLIKSi items and one for all BSSI items.

The median age of onset (median absolute deviation) for all PEs was 14.0 (3.0). Median onsets for hallucinations, delusions and anomalous experiences were 14.5 (2.2), 14.0 (3.0) and 15 (1.5), respectively. Neither medians nor histograms suggested difference in age of onset by specific modality, confirmed by non-significant one-way Kruskal-Wallis ANOVA ($chi^H = 0.27$, df = 2, p = 0.87).

5.4.2 Analysis Set 2: Analysis of underlying latent variables

Latent variable model comparison: AEB, PI & PEs

Table 5.4 shows the fit indices from full-information MLR models of AEB, PI and PEs items.

AIC, BIC and SABIC favoured the model with a general factor and an orthogonal specific factor for each item type (verified, self-report AEB and self-report PI). However, when I re-estimated this model with a WLSMV estimator, the variances of one of the BSSI-PI items was negative. This tends to occur when a model is mis-specified, such as an item loading on too many indicators and leaving no residual variance, or when one of the indicators is overly influential. The negative variance persisted when re-estimating the model, so it is unlikely to be due to sampling error. This negative variance made the results of this model inadmissible.

The next winning model was the bifactor model with two specific factors, one explaining covariance among verified interview items and one explaining variance in all self-report items.

When estimated with a WLSMV estimator, there were no negative variances and the model fit was excellent (N = 921, CFI = 0.987, TLI = 0.982, RMSEA = 0.035). The only difference between the best and second-best fitting models was the composition of specific factors, which are of little interest here.

Parameter estimates of the winning WLSMV-estimated bifactor model are given in Appendix B. The loadings of the interview items on their specific factor were non-significant, indicating that there is not much information remaining in these items after accounting for the general factor.

Table 5.5: Results of comparison of different model structures fit to combined interview and self-report PEs

Model	AIC	BIC	SABIC
Unidimensional	9362.08	9496.16	9410.40
Two Correlated Factors	9227.73	9366.78	9277.84
Two Uncorrelated Factors	9253.76	9387.84	9302.08
Bifactor	9197.29	9376.07	9261.73

Table 5.5: Results of model comparison of competing structures fit to interview-verified PEs and self-report social anxiety using fit indices that trade-off model fit with model parsimony. Lower values indicate better fit. The winning model was the Bifactor model, followed by two correlated factors.

Similarly, 5 of the 13 loadings of the self-report items on their specific factor were non-significant. However, loadings of some items were significant. This indicates that these items share some significant covariance that is orthogonal to that explained by the general factor.

The MLR-estimated winning bifactor model fit the data well (CFI = 0.940, TLI = 0.918, RMSEA = 0.04). I therefore used this model to calculate approximate ω statistics.

Approximate ω statistics indicated that a large amount of variance was explained by the general factor. For the general factor, ω_{H} indicated that 77.5% of the variance in the items was explained by the general factor. The specific factors explained less of the variance; ω for the verified-item specific factor was 1.7%, supporting that there is little information remaining in these items. ω for the self-report item specific factor was 7.9%, reflecting that this factor still captures some variance in the self-report items.

A conservative estimate of ω_{T} was 87.1%, suggesting good internal consistency. Measurement error accounted for 12.9% of the variance.

ω_{H} estimated for the general factor from the WLSMV model, properly adjusted for categorical items, was 89.6%, with bootstrap 95% confidence intervals of 81.4% – 92.0%. This strongly supports a common psychosis factor underlying self-report and verified items.

Latent variable model comparison: SA & PEs

Table 5.5 shows the results of MLR-estimated model comparison. BIC favoured the two-correlated-factors model over the bifactor model, while AIC and SABIC favoured the bifactor model. However, the bifactor model did not converge when fit to categorical data with a WLSMV estimator, while the WLSMV-estimated two-correlated-factors model converged and showed excellent fit (CFI = 0.999, TLI = 0.998, RMSEA = 0.027). This supports specificity of the associations between AEB, PI and interview-verified PEs.

Figure 5.3: Thresholds estimated from bifactor model of combined self-report and interview PEs items

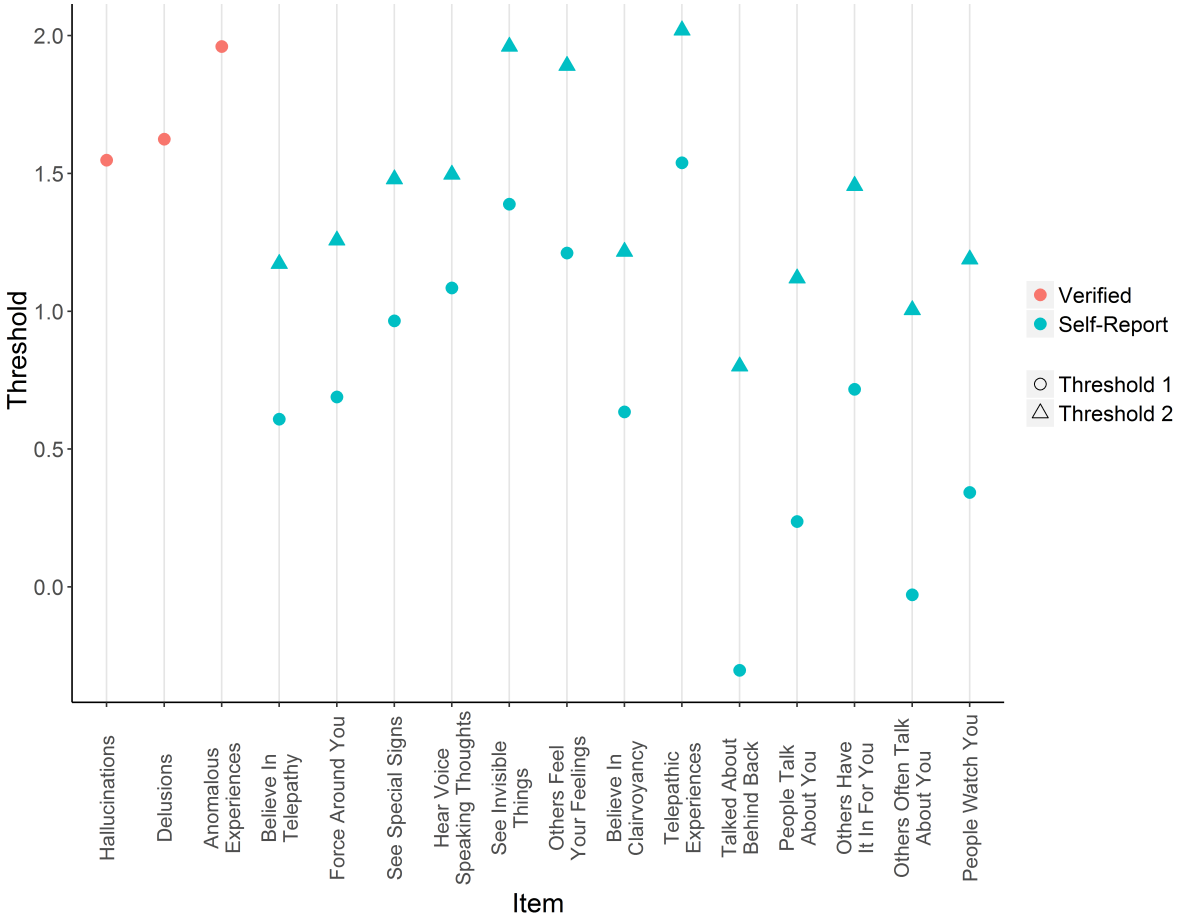


Figure 5.3: Thresholds (level of the latent variable at which a different categorical response is emitted) for interview and self-report items. Interview items had high thresholds but fell within the range of the self-report thresholds. Some self-report items had far lower thresholds, extending measurement to lower-severity psychotic phenomena.

Measuring different levels of psychosis severity (I): item threshold comparison

I extracted the item thresholds estimated from this bifactor model (Figure 5.3). The thresholds for verified interview items were high, with anomalous experiences ranking joint second-highest with the 'Sometimes/Mostly/Always' threshold for "Have you seen things invisible to other people?", delusions ranking fifth highest and hallucinations ranking sixth highest.

However, these thresholds were all within the range of the self-report thresholds. Furthermore, the lowest self-report threshold (from 'Not at all' to 'Occasionally' for item "I am sure I am being talked about behind my back") was 1.85 standard deviations of the latent trait below the lowest verified item threshold.This suggests that the self-report items measure a range of psychosis severity from a similar upper limit to the verified interview items down to a far less-severe lower limit.

Figure 5.4: Information distributions for self-report and interview items

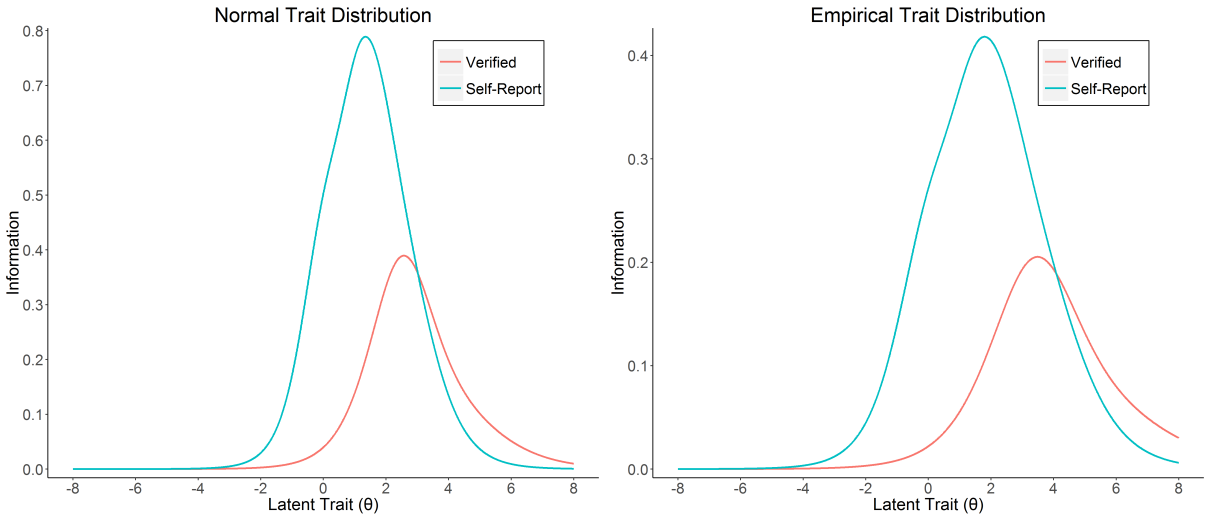


Figure 5.4: Information distributions were estimated using parametric item response theory analyses with two-parameter logistic curves. The curves quantify where along the distribution of a latent trait an item contributes information and thus is able to measure PEs. Interview items uniquely measure a slightly more severe range of PEs than self-report items but self-report items uniquely measure far less severe range of psychotic phenomena. The distributions were very similar for both traits assumed to have a normal distribution and empirically-estimated distributions.

Measuring different levels of psychosis severity (II): test information distributions

Two unidimensional IRT models were fit to all verified and self-report items, as an approximation of the general factor, one with the conventional assumption of a normally distributed latent trait and the other using a histogram method to construct a prior distribution of the latent trait empirically. Information distributions across the latent trait range were calculated for each item and summed for self-report and interview items separately.

Wilcoxon rank-sum test on the AUC values of the item information distributions showed that self-report items contributed more information, on average, than verified items (Normal trait distribution: self-report mean AUC = 2.68 & SD = 0.91, verified mean AUC = 1.27 & SD = 0.33, W = 38, p = 0.007; empirical trait distribution: self-report mean AUC = 1.94 & SD = 0.67, verified mean AUC = 0.88 & SD = 0.30, W = 38, p = 0.007). Examining information distributions (Figure 5.4), it is evident in both solutions that verified items do contribute information to the higher severity range of the latent trait and slightly extend that range further than the self-report items.

However, the self-report items measure a broader range of severities at lower levels that are not measured by verified items at all. This is consistent with the item thresholds estimated from latent variable modelling. Furthermore, the verified items uniquely measure a slightly more severe range.

5.4.3 Supplementary results: Concurrent associations between self-report PEs and depressive symptoms

In both cohorts, I replicated the finding that a common distress factor explained variance in both PEs and classical depressive symptoms, with PEs measuring more severe distress (Appendix C).

5.5 Summary

In a representative population sample, I found prevalence of PEs to be comparable to other studies, if slightly higher than meta-analytical estimates. The majority of PEs were not attributable to sleep, drugs or illness and, contrary to expectations, were reported to have persisted for at least one year. People often only experienced a single modality of PEs, but having PEs in one or two modalities increase the odds of having them in another modality.

Most PEs reported at this age have their onsets in early-mid adolescence, with age of onset related to persistence. Single experience or shorter duration PEs tend to have onset more recently than persistent ones. Inference is complicated by retrospective reporting from a single measurement. The relationship between earlier onset and persistence may be because more recent PEs have not had time to persist for over one year; some of the PEs lasting for weeks/months at 17, with median onset of 16, may become PEs that persist for years if allowed more time. However, it was rare for adolescents with long-lasting PEs not to have at least possibly experienced PEs in the past year, suggesting little evidence of persistent PEs early in adolescence that then subsided, though recall may be biased against such experiences.

I then compared the measurement properties of unverified self-report and verified interview-assessed psychotic phenomena in a large general population sample of adolescents. As predicted, I found strong evidence for a common psychosis factor underlying self-report measurement of anomalous experiences & beliefs (AEB), paranoid ideation (PI) and interview-verified hallucinations, delusions and anomalous experiences. Contrary to predictions, most of the severity range measured by interview-verified PEs was also measured by self-report items. Consistent with predictions, interview items did measure severe psychosis-proneness and uniquely measured a small, very severe range that was not measured by self-report items. Self-report items uniquely measured a broad lower-severity range of the psychosis distribution.

5.5.1 Strengths and limitations

This study was strengthened by use of a large, representative cohorts of young people, use of latent variable model comparison, specificity (with respect to social anxiety), careful handling of missing data and thorough psychometric validation using multiple techniques. The study was limited by the fact that the BSSI is an uncommonly-used instrument that only measures PEs over the past two weeks and there being slightly more missing data on the BSSI than the PLIKSi.

Chapter 6

Discussion: The measurement of psychotic experiences in the general population

6.1 Summary of findings

I review the main findings, strengths and limitations of each study below, with reference to my research questions. I then discuss the implications of these results for the measurement, dimensionality and health implications of PEs and how I could build on these results by investigating their aetiology and mechanisms.

6.1.1 General strengths and limitations

All studies were strengthened by use of large, representative or near-representative cohorts of young people. All studies were limited by use of self-report instruments, though questions in Chapter 2 and 3 related specifically to comparison of interview and self-report instruments and replication of previous findings with interview measurements, respectively.

6.1.2 Question 1: Do existing theories of schizotypy account for dimensionality of PEs and related traits in young people? How well can we measure PEs with self-report instruments?

I began by investigating the measurement of PEs and personality characteristics traditionally grouped together as 'schizotypal' traits. I identified the optimal latent dimensional structures of two instruments measuring self-report PEs and schizotypal traits in adolescence. The optimal structure was defined as whatever best traded-off fit to observed data with model parsimony and reliability of measurement. The optimal structure of the Brief Schizotypal Symptoms Inventory (BSSI) (Hodgekins et al., 2012a) was similar to existing models, while a novel 6-factor structure of the Schizotypal Personality Questionnaire (SPQ) (Raine, 1991) outperformed all existing

dimensional structures and improved measurement precision. This was similar to factorial structures identified using similar techniques in a smaller sample of undergraduates (Chmielewski and Watson, 2008). The largest (in terms of numbers of items) and most relevant factors for study, measuring asociality and interpersonal difficulties (Aso), paranoid ideation (PI) and non-paranoid anomalous experiences and beliefs (AEB) showed strong measurement invariance over age and sex. This lends strong support to a 6-factor model of schizotypal traits.

6.1.3 Question 2: Do instruments designed to measure different theoretical conceptualisations of PEs measure the same underlying phenomena in young people? If so, do they measure the same or distinct severity ranges of PEs?

In Chapter 5, I showed that interview and self-report measurements of PEs measure a common underlying factor. This was specific to anomalous experiences & beliefs and paranoid ideation; two distinct factors explained pooled data on interview-verified PEs and self-report social anxiety. This lends support to a generalised approach to PEs, such as in the 'extended psychosis phenotype' (van Os and Reininghaus, 2016) approach, and suggests that instruments arising from different traditions are measuring a common underlying system. While this study was not intended to address questions of the shape or taxonicity of the extended psychosis phenotype, it indicates that variation in the severity of PEs in the general population can be satisfactorily modelled as a continuous distribution (though it may truly be a series of discontinuous populations (Linscott & van Os, 2010)). It supports the synthesis of work from different domains such as schizotypy and psychosis-risk populations, though clearly these findings would need to be replicated for other instruments and populations.

These results also support the validity of self-report psychotic phenomena to measure the distribution of PEs in the general population of young people. In particular, the finding that self-report items are better at measuring lower severity psychosis-proneness, including around the population mean, may have important implications for future empirical work. The full distribution of intensity or severity of psychotic phenomena is poorly captured by interview instruments alone. Combining self-report and interview measurements can provide finer-grained discrimination of individuals by their levels of psychotic phenomena. This may be very relevant when attempting to identify genetic (Xu et al., 2015) and environmental aetiological factors and cognitive or brain mechanisms of psychotic phenomena.

This study was strengthened by use of latent variable model comparison, specificity (with respect to social anxiety), careful handling of missing data and thorough psychometric validation using a number of techniques. The study was limited by the fact that the BSSI is a fairly uncommon instrument that only measures PEs over the past two weeks and there being slightly more missing data on the BSSI than the PLIKSi.

6.2 Discussion

Together, the results of Chapters 6 and 5 provide important information on how PEs are measured in the general population and what measurements of PEs by traditional instruments reflect.

Compared to interviews, self-report instruments may extend the severity range measured towards the less-severe end of the distribution. Importantly, the BSSI could still measure almost as severe PEs as the PLIKSi, lending support to the use of this instrument and suggesting there is a distribution of PEs in the general population, with phenotypic continuity between less and more severe PEs.

A key question is whether phenotypic continuity of PEs arises from continuity in underlying mechanisms in terms of information-processing and its neurobiological implementation. Mild and more severe PEs share aetiological factors (Zavos et al., 2014), implying mechanistic continuity. However, this will remain an open question until it is tested directly by large-scale computational and neurobiological phenotyping (Friston et al., 2014) across the breadth of the psychosis distribution.

If lower-severity psychotic phenomena are phenotypically and mechanistically continuous with more severe psychosis, research using psychosis-prone people in the general population could generate predictions about clinical psychosis and aid in the search for biomarkers for psychotic disorders. If the lower severity range are phenotypically continuous but mechanistically discontinuous, it may enable classification of psychotic phenomena into likely clinical relevance based on underlying mechanisms.

If we are to test whether the same mechanisms exist across the distribution of PEs and even across clinical psychosis, we need to ensure we know what severity range we are measuring. Comparing populations based solely on a binary interview measure, like those experiencing verified PEs versus not, may be reliable and comparable to clinical measurement but it is blind to variability at the lower-severity range that may be valuable in individual differences studies or stratified sampling. PE-like phenomena that fall below the threshold on an interview measure are also unlikely to be purely measurement error, but rather capture meaningful variability with potential clinical relevance (van Nierop et al., 2012).

Similarly, measuring the lower severity range may allow us to identify the effects of risk and protective factors, such as drug use or social support, on psychotic phenomena more sensitively than comparing whether verified PEs are present or absent. However, further work is necessary on the shape of the distribution of psychosis severity (and other related factors). If, for example, an intervention reduces the severity of psychotic phenomena but is not able to move people over a threshold or step in the distribution of risk or need for clinical care, its clinical value may be limited.

The results of this study may explain why instrument type has such a large effect on estimates of PE prevalence in the general population. Different instruments and items may all be measuring the same underlying psychosis distribution(s), but with varying response thresholds that define the mappings from 'true' levels of psychosis-proneness to observed measurements. Pooling prevalence estimates from instruments with a wide range of threshold values will of course

introduce huge variability. This does not fundamentally compromise self-report instruments, but does require careful consideration of what severity of PEs they are really measuring. Similarly, self-report items may have low positive-predictive value for PEs (Horwood et al., 2008) partly because they have different response thresholds. Conversely, some self-report items are good predictors of interview-verified PEs (Kelleher et al., 2011), which may in part arise because these items have similar thresholds.

In these studies, I have discussed and mathematically modelled a distribution of psychotic phenomena in the general population. However, ambiguity remains over what exactly is distributed about a distributed psychosis phenotype (David, 2010; Lawrie et al., 2010). My results cannot speak to the complex question of whether this is continuous with clinical psychosis (Lawrie, 2016) and whether this distribution is specifically related to psychotic disorder versus nonpsychotic disorders (Kounali et al., 2014). We can, however, attempt to interpret what phenomenological properties make experiences or beliefs more or less 'psychotic'. While I modelled a general factor underlying various dimensions of PEs, various properties of PEs may exist as correlated distributions, like their frequency, their persistence, their vividness or intrusiveness or the distress and impairment they cause. Some recent self-report instruments capture these properties explicitly (Peters et al., 2004; Bell et al., 2006). Many older instruments, particularly those arising from personality and individual differences research, capture these dimensions implicitly by the phrasing of statements or questions. The latent factor estimated from agreement or disagreement with these statements is really a model of item covariance and its meaning must be interpreted from the statements and the relationships between them, captured by their loadings and thresholds.

Using variously phrased statements and questions can make it difficult to rigorously define the psychosis distribution. For example, item thresholds show that it takes a higher level on the distribution to even 'occasionally' (first response threshold) respond that you see things invisible to other people than it does to say that you 'sometimes', 'mostly' or 'all of the time' (second response threshold) believe in clairvoyancy or think that people talk about you behind your back. This is broadly consistent with an increasing aberrance of subjective experience from social or cultural norms with interestingly reliable content between individuals, such as people reading your thoughts or conspiring against you. The distribution estimated here has elements of how malign or threatening the experiences are (e.g. thresholds model people talking about you, then watching you, then 'having it in for you' as being progressively more 'psychotic'), how frequent they are (e.g. the more frequent thresholds are higher than the less frequent thresholds) and how much conviction or personal experience you have of them (e.g. thresholds suggest believing in mind-reading is far less 'psychotic' than reporting actual telepathic experiences). However, we cannot separate these aspects, we do not know which of them are the most impairing and we could not use this measurement to investigate if they have different mechanisms or aetiological factors. Newer generations of psychometric instruments and careful study design may make it possible to specifically define what exactly is distributed about psychosis and how those distributions map onto computational and brain mechanisms and aetiological factors. Carefully specified theories of what is distributed about psychosis and, critically, instruments that can reliably and validly measure those distributions, will be essential for future research into psychotic experiences occurring in and outside of psychotic disorders.

For synthesis of psychiatric research that uses a great variety of instruments, studies such as this are necessary to establish how measurements made by different instruments map onto an underlying psychosis-proneness distribution and on to one another, establishing inter-instrument reliability. Improving the precision of measurement of psychosis phenotypes will enable testing of more sophisticated hypotheses and, hopefully, lead to better understanding of their underlying mechanisms.

This is further complicated by my findings that some of the variance in PEs is shared with depressive symptoms. The common distress factor is potentially troubling for empirical studies, particularly those that investigate paranoid ideation because some of the variance in sum score measurements is non-specific variance in distress that will manifest as (at least) depressive symptoms, anomalous experiences/beliefs and paranoid ideation. In Appendix C, I estimated this proportion of non-specific variance to be 0.35-0.44 for anomalous experiences/beliefs and 0.88-0.91 for paranoid ideation. While I did not empirically test this, it is possible that the general factor explaining shared variance in depressive symptoms and PEs would be highly related to a general factor explaining, for example, shared variance in depressive symptoms and anxiety (Brodbeck et al., 2011) or overlap in psychiatric diagnoses (Caspi et al., 2014). When a variable like performance on a behavioural task is found to be associated with paranoid ideation or unusual perceptions without testing associations with other symptom dimensions, it would not be possible to ascertain whether the relationship is specific to psychotic phenomena or reflects either a stronger relationship with a different, correlated symptom dimension or a relationship with all overlapping symptom dimensions. When trying to uncover the mechanisms or aetiology of a particular symptom dimension, these results emphasise that it is critical to either estimate proportions of shared and unique variance using latent variable modelling or simultaneously investigate different symptom dimensions and look for specificity of relationships, i.e. mechanism A is associated with symptom dimension X and not symptom dimension Y, with the association between A and X being greater than the association between A and Y. The former method is likely to be impractical due to requirements for large sample sizes but the latter method can easily be implemented.

In terms of information-processing, PEs might index high levels of distress because extreme negative affect or psychosocial stress shift the parameters of perceptual inference and belief updating, in favour of aberrant inference of the causes of sensory data from prior expectations (hallucinations/delusional appraisals), aberrant updating of internal models from prediction errors (delusion formation) and overgeneralisation or overweighting of high-level beliefs to explain low-level prediction errors (delusion persistence).

More generally, aberrant beliefs form a troubling part of most psychiatric disorders, such as global negative beliefs about the self and the world that characterise depression (Friston et al., 2014). The aberrant updating and use of internal models about the world may therefore be a common computational mechanism that tends towards psychiatric disorder. Suggestions of common psychopathology factors have been criticised by indicating that, whatever the validity of current diagnostic systems, the same treatments, particularly psychopharmacological treatments, do not work for all patients (Lawrie et al., 2010). For example, response to lithium is quite different in someone diagnosed with a bipolar disorder as someone with nonaffective psychosis. These criticisms are levelled at a model where the common psychopathology factor is the same

at every level of explanation, which is unlikely. Rather, aberrant beliefs and aberrant inferences, which might in extremis generate psychotic experiences, may be a point of convergence of many disorders at the level of information processing. Those computational changes could be underpinned by divergent changes to the physical implementation of information-processing, hopefully distinguishable by neurobiological investigation, and may be caused by divergent genetic and environmental factors.

Chapter 7

Psychotic experiences with and without distress in two cohorts of adolescents and young adults

Abstract

In this chapter, I investigated whether psychotic experiences (PEs) occurred with and without distress and risk of mental disorders in the general population of adolescents and young adults and what environmental factors differentiated PEs with and without distress. Clusters of participants with self-report PEs and depressive symptoms (DS) were identified using latent class analysis (LCA). The number of clusters were identified with the bootstrap likelihood ratio test (BLRT) and AIC/BIC. Data came from two general population cohorts (ROOTS: N = 1056, age 17; NSPN: N = 2388, age 14-25, split into 3 age bins, a: 14-16, b: 17-19, c: 20-25). I compared clusters with distress and PEs (DPE), clusters that were non-distressed with PEs (NDPE) and 'reference' clusters without distress or PEs. Lifetime and current risk of common mental disorders and PEs were verified in ROOTS using interview assessments. Mental health was verified in NSPN using self-report lifetime and current help-seeking for any mental disorder. The environmental factors investigated were: cannabis use, childhood adversity, recent social support from friends and family (both cohorts) and schizotypal personality (NSPN). BLRT favoured 6 clusters in ROOTS and NSPN a & c and 5 clusters in NSPN b. 6-cluster models also performed well on AIC and BIC and were selected for further analysis. The predicted clusters were identified with similar prevalences in each LCA (Reference: prevalences = 62.8%, 50.8%, 45.6%, 49.8% of Cohorts 1 & 2a-c, respectively; NDPE: prevalences = 9.4%, 15.3%, 7.5%, 13.1%; DPE: prevalences = 5%, 10%, 8.8%, 4.5%). DPE and NDPE clusters were equally likely to have non-paranoid unusual perceptions and beliefs (all samples) and interview-verified hallucinations and bizarre experiences (ROOTS). DPE clusters had higher paranoid ideation (all samples) and interview-verified delusions (ROOTS), compared to NDPE. DPE had increased lifetime and current risk of mental disorders compared to reference and NDPE clusters (all samples). NDPE also had increased lifetime mental disorders compared to reference in ROOTS & NSPN-c. Childhood adversity and cannabis use were similarly associated with both PE clusters. Social support from family and friends was far greater for NDPE than DPE; NDPE had similar social support to reference (all samples). DPE had more asocial schizotypal traits (NSPN). These results show PEs occur with high distress and high risk of mental disorders in some young people, but low distress and low/modest risk of mental disorders in others. PEs without dis-

tress did not appear to simply be mild/attenuated PEs but tended not to feature paranoia or delusions. Some environmental factors may predispose similarly to PEs with and without distress, while social support and social functioning may be critical in determining health trajectories in young people with PEs.

7.1 Research Questions

- Do PEs always co-occur with other symptoms of psychopathology in young people in the general population or can they occur without symptoms of distress or functional impairment?
- What factors differentiate between PEs with and without distress?

7.2 Introduction

Psychotic phenomena occurring in the general population are a risk-indicator for psychotic (Fusar-Poli et al., 2013) and non-psychotic (Fusar-Poli et al., 2014a) illnesses. Interview-measured psychotic experiences (PEs) and self-report depression-like and anxiety-like symptoms can be well explained by a bifactor latent variable model, in which a general distress factor explains some of the variance in all psychosis and distress items (Stochl et al., 2015). When examined using item response theory analysis, psychotic experiences uniquely measure a more severe range of the general distress factor, not measured by traditional symptoms of depression and anxiety.

At the same time, PEs have been conceptualised as a normal, potentially benign aspect of personality (Claridge and Beech, 1995; Mohr and Claridge, 2015). Evidence for benign psychosis-proneness has been disputed (Lenzenweger, 2015), though a recent study showed that even persistent psychotic phenomena, phenomenologically similar to symptoms of clinical psychosis, can occur without need for clinical care (Peters et al., 2016a). Such people tend to have positive appraisals of their PEs and might consider them beneficial for wellbeing.

I would argue this represents a paradox; how can psychotic phenomena index severe distress as well as be a benign aspect of experience in some people? Importantly, these two conceptualisations of psychosis-proneness in the general population motivate quite different courses of action when PEs are identified. The former suggests that there may be a benefit in screening and even intervening in the psychosis-prone general population while the latter suggests that PEs in some people may not require intervention or medicalisation. Recognising that PEs are not necessarily a disease symptom strengthens the case for modern psychological therapies that facilitate positive appraisals, normalisation and acceptance of psychotic phenomena (Morrison and Barratt, 2010; Chadwick, 2014). In Appendix C I replicated, in two cohorts and with different instruments, that: firstly, a 'common mental distress' factor underlies and explains most of the variance in psychotic phenomena and depressive/anxious symptoms and, secondly, psychotic phenomena measure more extreme distress than classical depressive/anxious symptoms. However, there was additional variance in psychotic phenomena orthogonal to distress, raising the possibility that PEs are associated with varying levels of distress.

This is supported by existing findings (Peters et al., 2016) but, critically, much of the evidence of nonclinical or 'benign' PEs comes from highly selected adult samples that are not representative of the general population. The prevalence of benign PEs in the general population is not known, nor is whether the nonclinical psychosis cluster is robust and replicable. Neither is there strong evidence of benign PEs of a similar intensity to clinical PEs in adolescents and young adults. This developmental period is thought to contain the onset of most of psychotic disorders (Kessler et al., 2007) and may be a critical period for both environmental insults and intervention (Birchwood et al., 1998), hence why so much effort is directed at predicting and modifying the course of psychotic illnesses in this age range (McGorry, 2011).

The existence of benign PEs in young people would be important for strategies aimed at early detection and prevention of psychotic disorders, as it may allow better stratification of risk. For some, this may avoid unnecessary intervention and investment of resources. However, if PEs reflect susceptibility to environmental stress or tendency towards atypical belief formation, even PEs occurring without distress might still be important predictors, perhaps non-specifically, of lifetime psychiatric risk, given that maladaptive beliefs are a transdiagnostic feature of mental illnesses (Friston et al., 2014), PEs precede and follow onset of many common mental illnesses (McGrath et al., 2016) and high-risk criteria for psychosis also predict non-psychotic illnesses (Fusar-Poli et al., 2012). Comparing benign PEs versus PEs with concurrent distress may reveal risk and protective factors that could improve prediction of disorder and present potentially modifiable intervention targets.

In this chapter, I used person-centred, data-driven analyses to cluster these same participants by depressive symptoms and psychotic phenomena, to test whether some PEs manifest without distress. I then went on to investigate the nature of these clusters in more detail to identify factors that might explain heterogeneity in health outcomes in psychosis-prone young people.

I focused on the following set of questions. First, do PEs manifest with and without distress in general population samples of adolescents and young adults and what proportion of the population display these symptom phenotypes? Specifically, I looked for evidence of: i) a 'distressed, PE-prone' cluster (DPE) with high levels of distress and psychotic phenomena; ii) a 'non-distressed, PE-prone' cluster (NDPE) with low levels of distress but high levels of psychotic phenomena and iii) a 'Reference' cluster, with low levels of distress and psychotic phenomena, to serve as a comparison.

Second, is the NDPE phenotype simply a mild or attenuated form of psychosis-proneness, compared to DPE? (David, 2010) Some have argued that nonclinical PEs (or 'psychosis-like experiences') are more transient and less severe than true psychotic symptoms (Stanghellini et al., 2012). While a number of studies have reported on persistent PEs in people without a need for care (Brett et al., 2007, 2014; Lovatt et al., 2010; Johns et al., 2014; Ward et al., 2014), none to my knowledge have done so in a representative population cohort of adolescents or young adults.

Third, what levels of mental disorders or help-seeking for mental illness are displayed by these different groups? The NDPE group may still be at increased risk of mental illness, relative to controls, suggesting that PEs tend not to be truly 'benign' but are distributed on a spectrum of associated psychopathology and functional impairment.

Fourth, are these groups distinguishable by sociodemographic factors, features of childhood and adolescent/adult social support and adversity, other symptoms, traits & wellbeing, current and past mental disorders/help-seeking for mental illness and education/employment characteristics? Comparing these groups may suggest risk and protective factors to use as predictors or intervention targets.

Finally, are patterns of manifestation of psychotic phenomena and distress the same across adolescence and young adulthood?

7.3 Methods

7.3.1 Data

Data come from the ROOTS and NSPN cohorts. For full information on the cohorts, see Methodology.

In the NSPN cohort, due to possible age differences in patterns of PEs and distress, the sample was split into three age bins: 14-16, 17-19 and 20-25.

7.3.2 Latent class clustering analysis

Latent class analysis is a form of finite mixture model-based analysis in which categorical observed variables are modelled as being caused by a latent (unobservable) categorical variable with a pre-specified number of classes, where each category is a different latent class (LC). The model assumes that, after accounting for the LC variable, the observed variables are locally independent. LC models were estimated using expectation-maximization (EM) maximum-likelihood. LC models can converge at local maxima, so each model was estimated 20 times with different random starting values and the model with the highest likelihood selected.

7.3.3 Instruments used for clustering

Self-report psychotic phenomena

In ROOTS, self-report psychotic phenomena were measured using the Brief Schizotypal Symptoms Inventory (BSSI) (Hodgekins et al., 2012), a 20-item self-report instrument measuring psychotic phenomena in the last two weeks. It measures three domains: Anomalous Experiences and Beliefs (AEB), comprising perceptual abnormalities and magical thinking (8 items); Paranoid Ideation (PI), comprising suspiciousness and ideas of reference (6 items); and Social Anxiety (SA, 8 items). One item from PI is redundant with another and was removed. The AEB and PI scales measure the same underlying psychosis factor as a semi-structured interview method (Horwood et al., 2008).

Questions were structured as a set of statements or questions. Participants indicated how often that statement applied to them in the last two weeks on a 5-point scale ('Not at all', 'Occasionally', 'Sometimes', 'Often' and 'All the time'. Due to low endorsement of some categories,

responses were collapsed into a 3-point scale ('Not at all', 'Occasionally', 'Sometimes/Often/All the time'). SSI scales are likely to be unidimensional (ω_H: SA = 0.65, AEB = 0.71, PI = 0.88) and have high internal consistency (ω_T: SA = 0.95, AEB = 0.93, PI = 0.93) (Revelle and Zinbarg, 2009).

In NSPN, self-report psychotic phenomena were measured with the Schizotypal Personality Questionnaire (SPQ) (Raine, 1991), which comprises 74 dichotomous items intended to measure general, trait-like experience of 9 dimensions associated with psychosis-proneness. In Chapter 1, I showed that, while these 9 dimensions are reliable, a number are likely to be redundant. While second-order latent variable models suggest three or four variables explain scores on these subscales, they are not reliable when estimated at the item level. Instead, I identified a reliable 6-factor solution without redundantly high correlations among factors. Of relevance for this study are the dimensions most similar to typical psychotic phenomena: 'Anomalous Experiences & Beliefs' (AEB), comprising 18 items measuring unusual perceptual experiences and magical thinking and 'Paranoid Ideation' (PI), comprising 13 items measuring suspiciousness and ideas of reference.

Verified psychotic experiences

PEs were measured in ROOTS using the semi-structured Psychotic-Like Symptoms Interview (Horwood et al., 2008) (PLIKSi). For further detail on the PLIKSi, see Chapter 5. Briefly, a modified version of the PLIKSi was administered to participants in schools and measured 17 types of PEs. PEs included were those that 'definitely', rather than 'possibly' occurred and were not attributable to sleep, illness/fever or substance use. For clustering, I used a binary variable of any lifetime PEs.

Depressive symptoms

In both cohorts, self-report depressive symptoms were measured with the Mood and Feelings Questionnaire (MFQ) (Costello and Angold, 1988). The full questionnaire comprises 33 items on common symptoms of depression and anxiety occurring over the last two weeks. The full MFQ is likely to be multidimensional (Brodbeck et al., 2011) and has more items than the AEB and PI scales of both the SPQ and SSI, which may pull any common factors estimated from combined psychosis and distress items towards measuring traditional distress and result in numerous specific factors. I therefore used the items that comprise the Short Mood and Feelings Questionnaire (SMFQ) (Angold et al., 1995), which are contained within the full MFQ. These items were used previously in identifying a common factor underlying mood, anxiety and psychotic experiences. The SMFQ is likely to be unidimensional and is able to predict clinical depression and anxiety with reasonable sensitivity (Messer et al., 1995; Turner et al., 2014).

Nonpsychotic psychiatric disorders/help-seeking

Current and past common mental disorders (a composite of depression, anxiety, eating disorders, obsessive-compulsive disorders and behavioural disorders) were measured in ROOTS at

age 14 and age 17 using the Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime version (Kaufman et al., 1997) (KSADS-PL). For clustering, I used a composite of adolescents who, at any time, definitely met criteria or showed significant, impairing symptoms ('High Clinical Index') but fell just short of the required threshold ('any lifetime mental disorder').

Summary

In ROOTS, I combined all 8 items from the AEB_{BSSI} scale and 5 non-redundant items from the 6-item PI_{BSSI} scale with the 13 SMFQ items, any lifetime PEs and any lifetime mental disorder, creating a pool of 28 items.

In NSPN, I combined the 18 items on the AEB_{SPQ} scale and 13 on the PI_{SPQ} scale with the 13 SMFQ items, creating a pool of 44 items.

7.3.4 Determining the number of classes

I fit models with varying numbers of classes and used AIC, BIC and the bootstrap likelihood ratio test (BLRT) to identify the most appropriate number of classes. AIC and BIC are comparative fit indices based on log-likelihood that trade-off model fit with model parsimony; lower values indicate better fit. The BLRT simulates, from observed data, a distribution of changes in log-likelihood that can be expected when one-too-many latent classes are estimated. The BLRT involved estimating a latent class model for a number of classes, n. I then simulated 500 datasets with n classes from this model and fit latent class models with n and n + 1 classes to each set. I calculated the likelihood ratio between the models for each set, constructing a null distribution of likelihood ratios that could be expected when there was no evidence for a greater number of classes. I then compared the true likelihood ratio in the observed data to this distribution. I used an alpha of 0.05 and obtained p-values by estimating the probability of observing the true likelihood ratio given the distribution of bootstrap likelihood ratios. I performed the BLRT for increasing numbers of classes until a non-significant result was observed, indicating no evidence for adding another class.

I examined the item response probabilities per latent class to investigate whether any clusters were interpretable as NDPE, DPE and Reference clusters.

7.3.5 Cluster comparisons

Clustering on population data was highly likely to return clusters of unequal sizes and distributions of variables of interest were likely to be of different shapes and variances across clusters. I therefore used robust statistical comparisons for all comparisons with continuous variables. For continuous variables, I used heteroskedastic one-way ANOVA on 5% trimmed means for omnibus tests (function *'t1way'*) with post hoc tests performed by Yuen's t-tests. Omnibus and pairwise comparisons between categorical variables were performed using χ^2 tests.

7.3.6 Follow-up comparisons of clusters

In each sample and for each clustering method, I compared NDPE, DPE and Reference clusters on a number of other variables. The number of comparisons made necessitated a 'classify-analyse' approach, though this can attenuate relationships between latent classes and other variables by ignoring uncertainty about classification.

Verified psychotic experiences

From PLIKSi data, I compared clusters in ROOTS on binary presence of any PEs persisting for at least a year and specific binary hallucinations, delusions and anomalous experiences.

Nonpsychotic psychiatric disorders/help-seeking

In ROOTS, I investigated when disorders occurred across clusters using variables of any current disorder at age 14 and any current disorder at age 17, measured using the KSADS-PL.

In NSPN, self-report current and past help-seeking for mental illness was measured as part of the postal questionnaire packs. I compared clusters on binary current help-seeking and lifetime help-seeking.

Sociodemographic characteristics

I compared clusters on sex, socioeconomic deprivation (estimated from post-codes in both samples; ROOTS: ACORN category of 'hard-pressed'
http://www.caci.co.uk; NSPN: z-scored Index of Multiple Deprivation,
https://www.gov.uk/government/collections/english-indices-of-deprivation) and non-white ethnicity.

Family psychiatric history

I compared clusters on any self-reported history of mental illness in first-degree relatives ('none' vs 'any').

Cannabis use

I compared clusters on cannabis use in the month prior to assessment ('none' vs 'any), measured as part of a drugs and alcohol screening instrument.

Childhood adversity and recent social support

I compared clusters in ROOTS on the number of adversities participants were exposed to between ages 0-14, measured using the Cambridge Early-Experiences Interview (Dunn et al., 2011)

(CAMEEI), a semi-structured caregiver interview measured at the first time point. In NSPN, adversity between ages 0-16 was measured using the self-report Measures of Parenting Style (Parker et al., 1997) (MOPS) questionnaire, with subscales of abuse, indifference and overbearingness measured for mothers and fathers independently. I used the total score of adversities from both parents.

Current perceived social support from friends was measuring using the Friendship Quality scale of the Cambridge Friendships Questionnaire (van Harmelen et al., 2016) (CFQ). Current perceived social support from family members was measured using the General Functioning scale of the McMasters Family Assessment Device (Epstein and Baldwin, 1983) (FAD).

Education and employment

In ROOTS, I compared clusters on number of secondary school qualifications (GCSEs) obtained, proportion of people doing higher education (A-levels) at 17 and proportion doing vocational training or education at 17. In NSPN, I compared clusters on proportions in full-time education, in full-time employment and proportions unemployed.

7.4 Results

7.4.1 Number of clusters

In ROOTS, AIC and BIC favoured 5 clusters, followed narrowly by 6 clusters. The BLRT warranted increasing the number of clusters from 5 to 6 ($p = 0.04$) but not 6 to 7 ($p = 0.09$). I therefore considered 6 clusters to be the optimal solution (see Table 7.1).

In NSPN, there was less clear evidence of an optimal number of clusters in each age group. To maximise comparability with ROOTS, I selected the 6-cluster solutions in all groups for further investigation. The 6-cluster solution performed well in all age groups (14-16: 3rd BIC, 3rd AIC, non-significant BLRT; 17-19: 3rd BIC, 3rd AIC, non-significant BLRT; 20-14: 1st BIC, 3rd AIC, non-significant BLRT, Table 7.1).

Table 7.1: Comparison of latent class clusterings with varying numbers of classes

Sample	N Clusters	BIC	AIC	BLRT p-value
ROOTS (17)	1	38317.46	38317.46	0
	2	34471.46	34471.46	0
	3	33800.68	33800.68	0.01
	4	33545.57	33545.57	0.04
	5	33452.9	33452.9	0.04
	6	33468.54	33468.54	0.09
	7	33583.48	33583.48	NA
	8	33779.16	33779.16	NA
NSPN (14-16)	1	36808.16	36550.15	0
	2	33565.43	33044.89	0
	3	33009.45	32226.37	0
	4	32589.28	31543.66	0.034
	5	32617.28	31309.12	0.018
	6	32736.82	31166.12	0.104
	7	32845.21	31011.98	NA
	8	33048	30952.23	NA
NSPN (17-19)	1	41964.09	41700.29	0
	2	37806.96	37274.73	0
	3	37322.9	36522.25	0
	4	36992.91	35923.83	0.056
	5	36864.27	35526.76	NA
	6	36924.59	35318.66	NA
	7	37027.14	35152.79	NA
	8	37247.95	35105.17	NA
NSPN (20-25)	1	49954.16	49678.49	0
	2	44798.53	44242.36	0
	3	43830.47	42993.8	0
	4	43345	42227.83	0.032
	5	43284.09	41886.41	0.044
	6	43260.22	41582.04	0.116
	7	43350.63	41391.94	NA
	8	43509.06	41269.87	NA

Table 7.1: Lower values of AIC and BIC indicate better performance. A significant BLRT indicates evidence for increasing the number of clusters. In ROOTS, AIC and BIC narrowly favoured 5 over 6 clusters, while BLRT favoured 6 clusters. In NSPN 14-16 and 20-25, BLRT favoured 6 clusters but 4 clusters in NSPN 17-19. AIC and BIC favoured different numbers of clusters though the 6-cluster models performed well. The 6-cluster model was selected as optimal.

7.4.2 Identifying and verifying Reference, NDPE and DPE clusters

Figure 7.1: ROOTS Latent class item probabilities probabilities

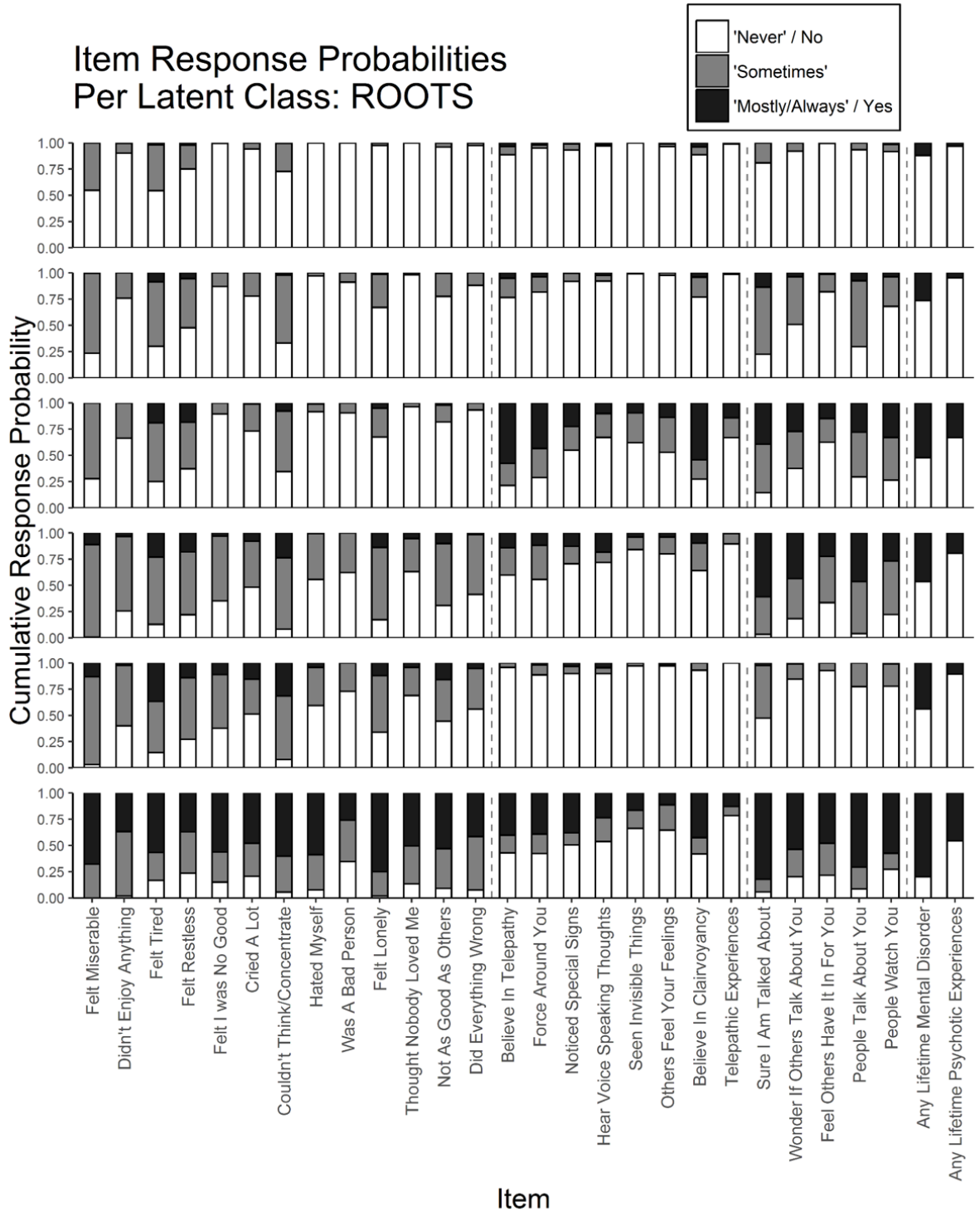


Figure 7.1: Bar heights indicate response probabilities for each latent class in ROOTS. Dashed bars separate item of different types. From left to right: depressive symptoms (13), anomalous experiences & beliefs (8), paranoid ideation (5), interview-verified psychotic experiences and mental disorders (2)

Figure 7.2: NSPN 14-16 Latent class item probabilities probabilities

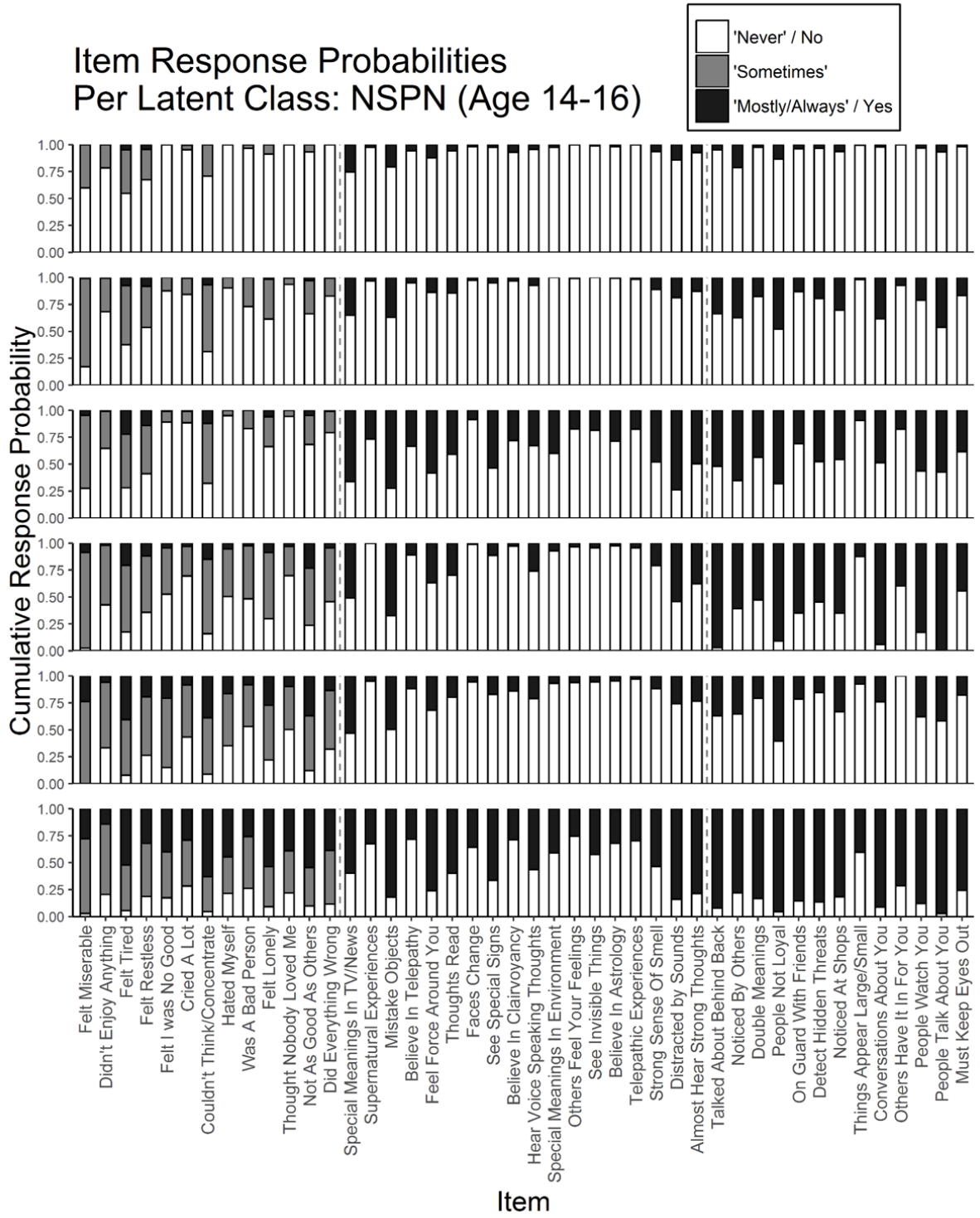


Figure 7.2: Bar heights indicate response probabilities for each latent class in NSPN 14-16. Dashed bars separate item of different types. From left to right: depressive symptoms (13), anomalous experiences & beliefs (18), paranoid ideation (13)

Figure 7.3: NSPN 17-19 Latent class item probabilities probabilities

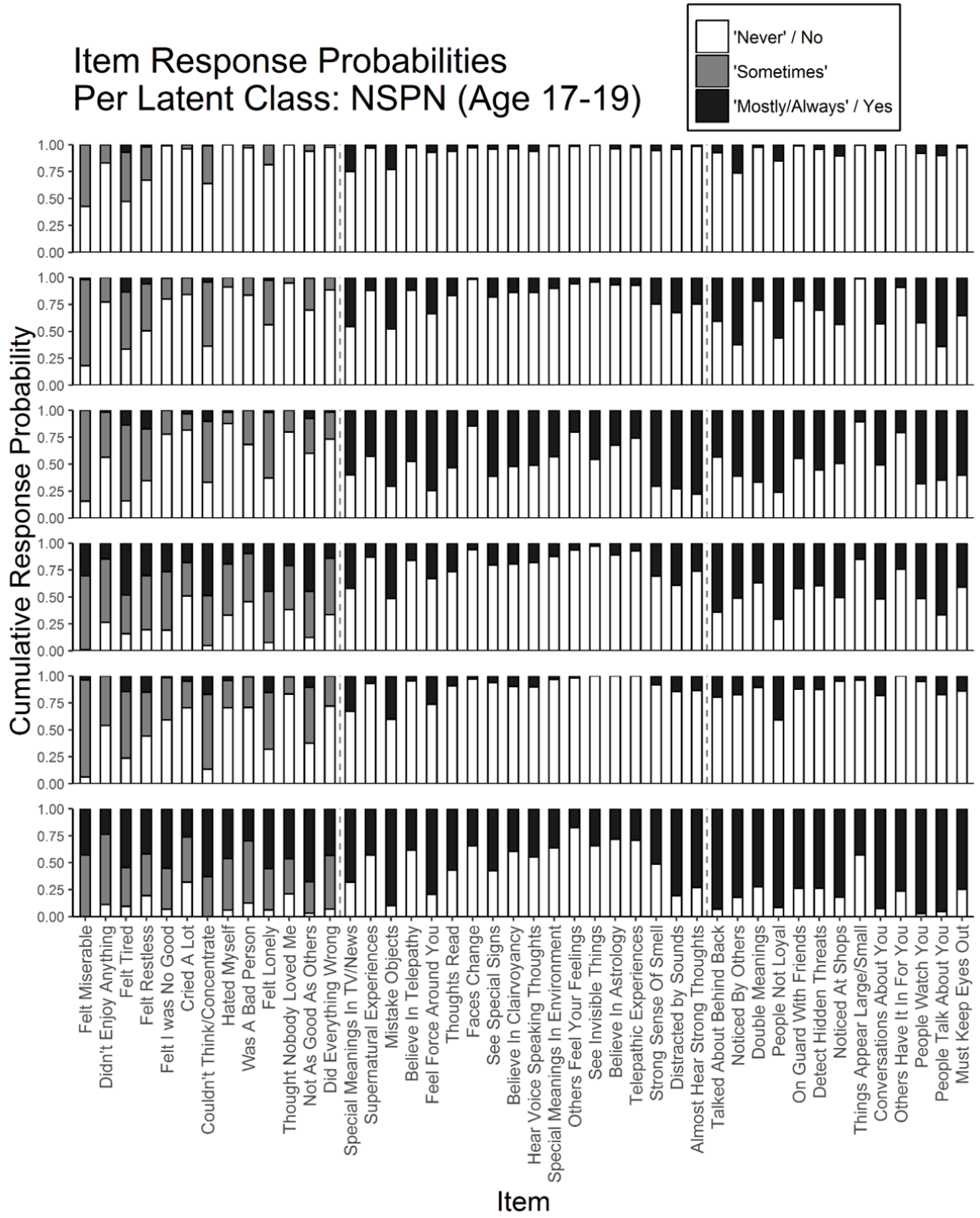


Figure 7.3: Bar heights indicate response probabilities for each latent class in NSPN 17-19. Dashed bars separate item of different types. From left to right: depressive symptoms (13), anomalous experiences & beliefs (18), paranoid ideation (13)

Figure 7.4: NSPN 20-25 Latent class item probabilities probabilities

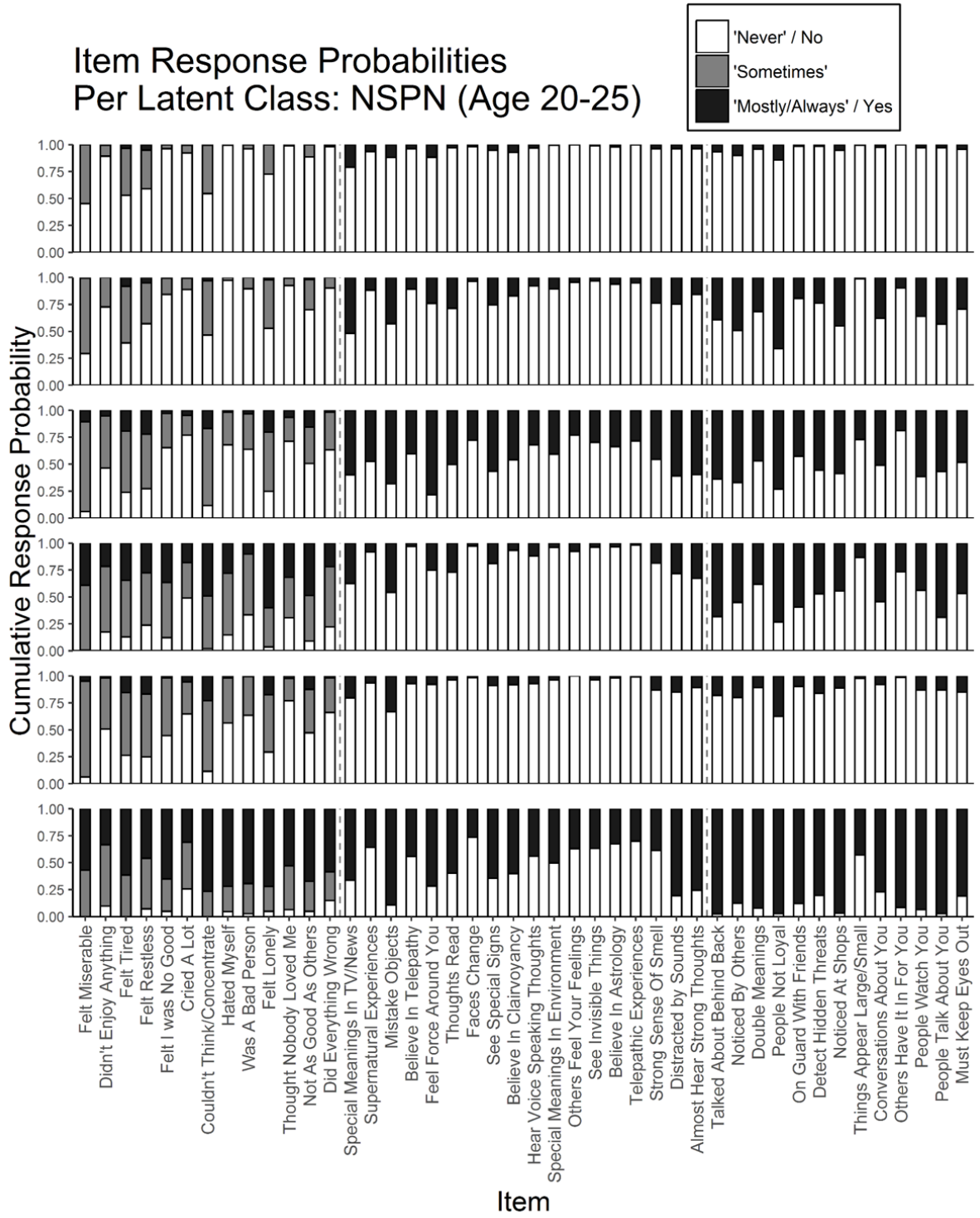


Figure 7.4: Bar heights indicate response probabilities for each latent class in NSPN 20-25. Dashed bars separate item of different types. From left to right: depressive symptoms (13), anomalous experiences & beliefs (18), paranoid ideation (13)

Item response probability plots for each cluster are shown in Figures 7.2 - 7.4. On inspection of the response probabilities, it appeared clusters were separated by levels of responses to all items on an instrument, rather than clusters of items within an instrument, meaning they could be characterised by total instrument scores.

In ROOTS, omnibus tests showed significant differences across clusters for these variables (DS: $F_{F(5,\ 211.8)} = 574.8$, $p < 0.001$; AEB: $F_{F(5,\ 211.3)} = 109.8$, $p < 0.001$; PI: $F_{F(5,\ 209.5)} = 359.2$, $p < 0.001$; lifetime PEs: ($\chi^2 = 112.4$, DF = 5, $p < 0.001$; lifetime mental disorders: : ($\chi^2 = 133.5$, DF = 5, $p < 0.001$).

In NSPN, omnibus tests for differences in DS, AEB, PI and help-seeking were all significant (14-16| DS: $F_{F(5,\ 218.3)} = 293.6$, $p < 0.001$; AEB: $F_{F(5,\ 214.3)} = 134.5$, $p < 0.001$; PI: $F_{F(5,\ 214.3)} = 705.1$, $p < 0.001$; Help-seeking: ($\chi^2 = 25.3$, DF = 5, $p < 0.001$| |17-19| DS: $F_{F(5,\ 226.1)} = 449.1$, $p < 0.001$; AEB: $F_{F(5,\ 224.9)} = 217.0$, $p < 0.001$; PI: $F_{F(5,\ 223.3)} = 446.1$, $p < 0.001$; Help-seeking: ($\chi^2 = 47.6$, DF = 5, $p < 0.001$| |20-25| DS: $F_{F(5,\ 229.7)} = 531.0$, $p < 0.001$; AEB: $F_{F(5,\ 204.7)} = 219.6$, $p < 0.001$; PI: $F_{F(5,\ 223.3)} = 719.5$, $p < 0.001$; Help-seeking: ($\chi^2 = 93.4$, DF = 5, $p < 0.001$).

In ROOTS, clusters 1 and 2 had extremely low and low levels, respectively, of DS, AEB, PI, PEs and mental disorders. Cluster 1 was considered the 'Reference' cluster (Ref). Cluster 3 had low DS but high AEB and moderate-high PI, PEs and mental disorders. Cluster 3 was considered the 'non-distressed, PE-prone' cluster (NDPE). Cluster 4 had moderate-high DS and mental disorders, moderate AEB and PEs and high PI. Cluster 5 had moderate-high DS and mental disorders but low AEB, PI and PEs. Cluster 6 had very high DS and mental disorders and high AEB, PI and PEs. Cluster 6 was considered the 'distressed, PE-prone' cluster (DPE).

In all NSPN samples, clusters 1, 2, 3 and 6 showed very similar symptom profiles to clusters found in ROOTS and clusters 1, 3 and 6 were considered the Reference, NDPE and DPE clusters, respectively. Clusters 4 and 5 were less coherent across all samples.

Figure 7.5: Bar plots of PEs and psychopathology markers per latent class

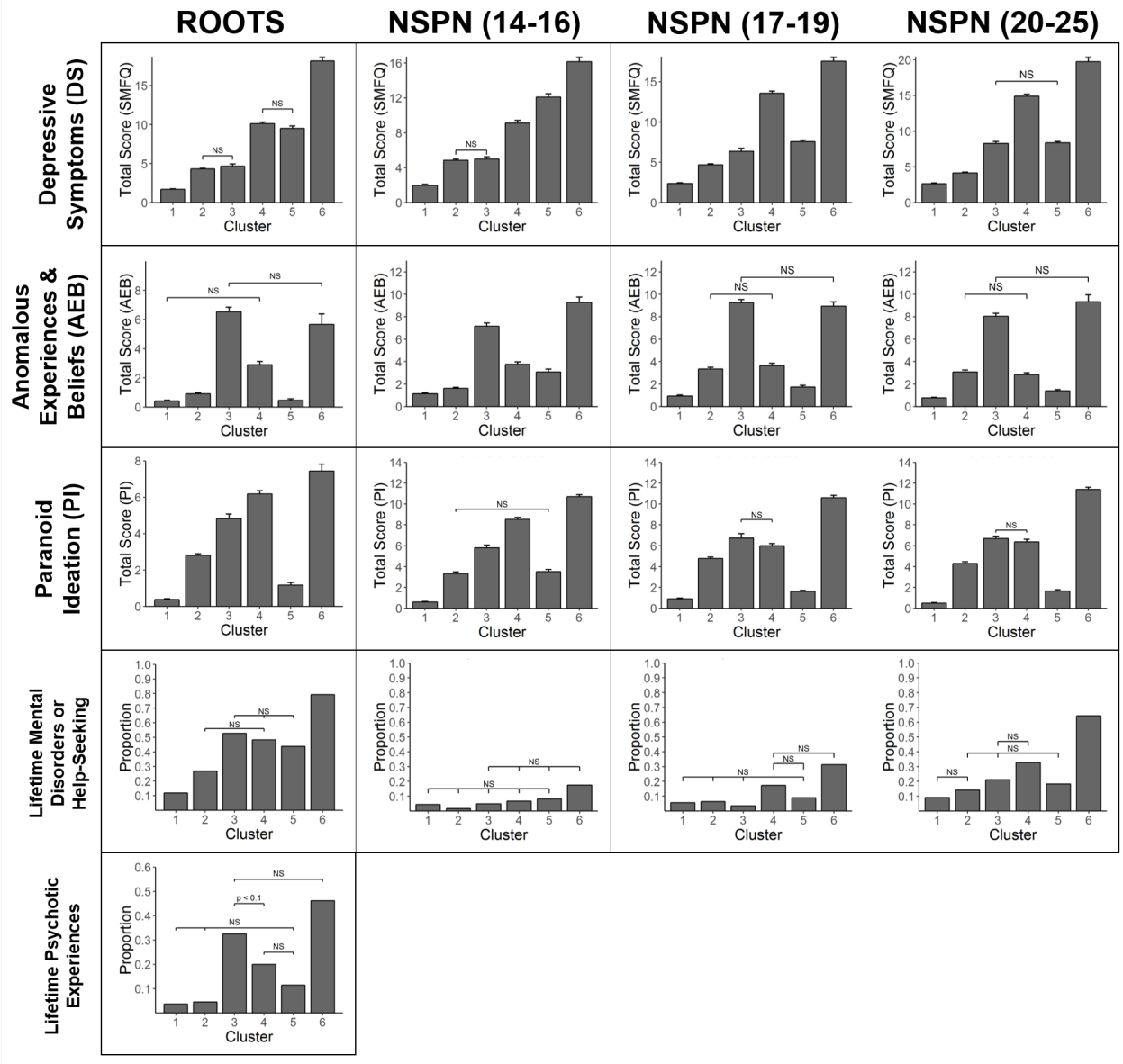


Figure 7.5: All omnibus tests showed overall differences. For clarity, horizontal bars marked 'NS' indicate non-significant differences on pairwise comparisons. Unmarked differences were significant at alpha of 0.05, Holm corrected.

The differences between clusters on sum scores of instruments used in clustering and on markers of psychopathology are shown in Figure 7.5. Replicable patterns of differences were found across each sample, particularly when comparing the Reference (Cluster 1), NDPE (Cluster 3) and DPE (Cluster 6) clusters.

7.4.3 Lifetime interview-verified PEs

In ROOTS, 32.6% and 53.8% of NDPE and DPE had verified lifetime PEs, respectively. NDPE and DPE had more lifetime PEs than all other clusters (though corrected p-value for NDPE $>$ cluster 4 indicated only trend-level difference). There was no significant difference between NDPE and DPE on lifetime PEs, suggesting similar levels of psychosis-proneness.

Table 7.2: Cluster sizes from 6-cluster latent class models

Cluster Number	ROOTS	NSPN 14-16	NSPN 17-19	NSPN 20-25
1 (Reference)	296 (30.7%)	158 (23%)	159 (20.9%)	284 (30.2%)
2	291 (30.2%)	191 (27.8%)	188 (24.7%)	184 (19.6%)
3 (NDPE)	89 (9.2%)	105 (15.3%)	57 (7.5%)	123 (13.1%)
4	145 (15.1%)	91 (13.2%)	167 (21.9%)	147 (15.7%)
5	89 (9.2%)	73 (10.6%)	123 (16.2%)	159 (16.9%)
6 (DPE)	53 (5.5%)	69 (10%)	67 (8.8%)	42 (4.5%)

7.4.4 Lifetime mental disorders or help-seeking for mental illness

In ROOTS, 79.2%, 52.8% and 11.8% of DPE, NDPE and Reference met criteria for one or more lifetime disorder, respectively. DPE had higher rates of interview-assessed lifetime mental disorders than all other clusters. NDPE had higher rates than Reference and cluster 2.

In NSPN, DPE had higher rates of help-seeking than Reference in all samples. The difference in help-seeking between DPE and all other clusters became more pronounced with age, (17.3%, 31.3% and 64.3% of DPE reported help-seeking in those aged 14-16, 17-19 and 20-25, respectively. This probably reflected increases in overall rates of help-seeking with age (14-16: 5.7%, 17-19: 11.0% and 20-25: 19.3%).

The sizes of each cluster in each sample are shown in Table 7.2. Of each sample, the Reference cluster comprised 20.9-30.7%, NDPE comprised 7.5-15.3% and DPE comprised 4.5-10%.

7.4.5 Comparison of Reference, NDPE and DPE clusters

Table 7.3: Follow-up comparisons of Reference, NDPE and DPE clusters in ROOTS

Variable	Instrument	Reference	NDPE	DPE	Omnibus	Pairwise Comparisons
Male	Self-Report	54.70%	34.80%	26.40%	$\chi^2 = 21.4$, DF = 2, p < 0.001	Ref > NDPE, Ref > DPE, NDPE = DPE
Non-White Ethnicity	Self-Report	4.80%	3.50%	6.10%	$\chi^2 = 0.5$, DF = 2, p = 0.788	-
Low Socioeconomic Status	ACORN Categories	11.50%	16.90%	18.90%	$\chi^2 = 3.2$, DF = 2, p = 0.788	-

Table 7.3 – continued from previous page

Variable	Instrument	Reference	NDPE	DPE	Omnibus	Pairwise Comparisons
Family History of Mental Illness	Self-Report	14.70%	24.10%	30.60%	$\chi^2 = 9.2$, DF = 2, p = 0.061	-
Cannabis Use	Drugs and Alcohol Screening Instrument	6.10%	16.90%	12%	$\chi^2 = 10.3$, DF = 2, p = 0.052	-
Any Current Mental Disorder at Age 17	KSADS-PL	3.70%	21.30%	52.80%	$\chi^2 = 100.8$, DF = 2, p < 0.001	Ref < NDPE < DPE
Any Current Mental Disorder at Age 14	KSADS-PL	5.10%	15.70%	17%	$\chi^2 = 15.1$, DF = 2, p = 0.006	Ref < NDPE, Ref < DPE, NDPE = DPE
Multiple Lifetime Mental Disorders	KSADS-PL	3.70%	30.30%	54.70%	$\chi^2 = 109.7$, DF = 2, p < 0.001	Ref < NDPE < DPE
Any Lifetime Hallucinations	PLIKSi	2.40%	19.10%	23.10%	$\chi^2 = 42.5$, DF = 2, p < 0.001	Ref < NDPE, Ref < DPE, NDPE = DPE
Any Lifetime Anomalous Experiences	PLIKSi	1%	9%	9.60%	$\chi^2 = 18.3$, DF = 2, p = 0.001	Ref < NDPE, Ref < DPE, NDPE = DPE
Any Lifetime Delusions	PLIKSi	0.30%	11.20%	30.80%	$\chi^2 = 75.6$, DF = 2, p < 0.001	Ref < NDPE < DPE
Any PEs persisting > 1 year	PLIKSi	1.40%	16.90%	17.30%	$\chi^2 = 39.1$, DF = 2, p < 0.001	Ref < NDPE, Ref < DPE, NDPE = DPE
Any PEs in the past year	PLIKSi	1.70%	22.50%	34.60%	$\chi^2 = 74.2$, DF = 2, p < 0.001	Ref < NDPE, Ref < DPE, NDPE = DPE
Anxious Symptoms (Age 17)	RCMAS	3.66 (3.9)	13.07 (8.37)	38.24 (7.78)	$F_{(2,83.7)} = 493$, p < 0.001	Ref < NDPE < DPE

Table 7.3 – continued from previous page

Variable	Instrument	Reference	NDPE	DPE	Omnibus	Pairwise Comparisons
Wellbeing (Age 17)	WEMWBS-14	41.51 (6.3)	39.04 (6.54)	29.02 (7.67)	$F_{(2,104.6)} = 63.6$, $p < 0.001$	Ref > NDPE > DPE
Depressive Symptoms (Age 14)	SMFQ	3.63 (3.32)	7.13 (5.37)	10.58 (5.3)	$F_{(2,80.9)} = 46.2$, $p < 0.001$	Ref < NDPE < DPE
Childhood Adversities	CAMEEI	1.21 (1.57)	1.82 (1.83)	2.22 (1.75)	$F_{(2,82.9)} = 8.1$, $p = 0.007$	Ref < NDPE, Ref < DPE, NDPE = DPE
Family Support (Age 17)	FAD (General Functioning)	29.85 (5.29)	27.86 (6.05)	21.63 (6.5)	$F_{(2,95.2)} = 35.6$, $p < 0.001$	Ref > NDPE > DPE
Friendship Support (Age 17)	CFQ (Friendship Support)	14.93 (1.99)	14.5 (2.6)	11.37 (4.07)	$F_{(2,87.5)} = 16.7$, $p < 0.001$	Ref = NDPE, Ref > DPE, NDPE > DPE
Family Support (Age 14)	FAD (General Functioning)	27.47 (5.21)	26.36 (5.01)	21.84 (6.75)	$F_{(2,91.4)} = 14.2$, $p < 0.001$	Ref > NDPE (trend), Ref > DPE, NDPE > DPE
Friendship Support (Age 14)	CFQ (Friendship Support)	14.41 (2.54)	13.51 (3.14)	12.32 (3.36)	$F_{(2,86.6)} = 10.2$, $p = 0.001$	Ref > NDPE, Ref > DPE, NDPE > DPE (trend)
Number of Secondary School Qualifications	Self-Report	8.32 (3.4)	7.61 (3.49)	7.62 (3.73)	$F_{(2,100.3)} = 1.7$, $p = 0.788$	-
In Higher Education at Age 17	Self-Report	71.60%	50%	62.30%	$\chi^2 = 14.4$, DF = 2, $p = 0.007$	Ref > NDPE, Ref = DPE, NDPE = DPE
In Vocational Education at Age 17	Self-Report	16.10%	29.50%	20.80%	$\chi^2 = 7.9$, DF = 2, $p = 0.097$	-

Table 7.4: Follow-up comparisons of Reference, NDPE and DPE cluster in NSPN 14-16

Variable	Instrument	Reference	NDPE	DPE	Omnibus	Pairwise Comparisons
Male	Self-Report	53%	61%	34.80%	χ^2 = 11.7, DF = 2, p = 0.017	Ref = NDPE, Ref > DPE, NDPE > DPE
Non-white Ethnicity	Self-Report	16.90%	30.50%	33.30%	χ^2 = 14.9, DF = 2, p = 0.004	Ref < NDPE, Ref < DPE, NDPE = DPE
Socio-economic Status	IMD	0.29 (0.99)	-0.14 (1.09)	-0.23 (1.11)	$F_{(2,128.7)}$ = 9.1, p = 0.002	Ref > NDPE, Ref > DPE, NDPE = DPE
Mental Illness in First Degree Relative	Self-Report	5.40%	5.70%	14.50%	χ^2 = 7.8, DF = 2, p = 0.104	-
Cannabis Use	Self-Report	5.20%	4.80%	10.10%	χ^2 = 2.9, DF = 2, p = 0.474	-
Lifetime Help-Seeking for Mental Illness	Self-Report	2.90%	4.80%	17.40%	χ^2 = 24.9, DF = 2, p < 0.001	Ref = NDPE, Ref < DPE, NDPE < DPE
Current Help-Seeking for Mental Illness	Self-Report	0.60%	2.90%	14.70%	χ^2 = 40.1, DF = 2, p < 0.001	Ref < NDPE (trend), Ref < DPE, NDPE < DPE
Depressive Symptoms	SMFQ	3.49 (2.29)	5 (2.63)	16.14 (4.45)	$F_{(2,120.2)}$ = 230.6, p < 0.001	Ref < NDPE < DPE
Anxiety Symptoms	RCMAS	9.92 (7.21)	15.31 (8.69)	37.92 (9.16)	$F_{(2,124.9)}$ = 274.7, p < 0.001	Ref < NDPE < DPE
Wellbeing	WEMWBS-14	46.64 (6.38)	45.02 (6.1)	31.62 (8.06)	$F_{(2,129.5)}$ = 105.5, p < 0.001	Ref > NDPE > DPE
Asociality	SPQ	2.84 (3.21)	4.87 (3.33)	10.68 (4.51)	$F_{(2,120.7)}$ = 84.7, p < 0.001	Ref < NDPE < DPE
Social Anxiety	SPQ	2.74 (2.26)	4.12 (2.28)	6.03 (2.28)	$F_{(2,130.8)}$ = 54, p < 0.001	Ref < NDPE < DPE

Variable	Instrument	Reference	NDPE	DPE	Omnibus	Pairwise Comparisons
Eccentricity	SPQ	1.3 (1.94)	3.37 (2.33)	5.88 (1.93)	$F_{(2,123.2)} = 143.7$, $p < 0.001$	Ref < NDPE < DPE
Odd Speech	SPQ	1.73 (1.6)	3.11 (1.57)	4.7 (1.38)	$F_{(2,142.5)} = 125.2$, $p < 0.001$	Ref < NDPE < DPE
Childhood Adversities	MOPS	4.79 (6.34)	10.34 (9.6)	18.26 (13.85)	$F_{(2,98.4)} = 38.3$, $p < 0.001$	Ref < NDPE < DPE
Family Support	FAD	39.3 (5.61)	36.88 (5.91)	29.55 (6.13)	$F_{(2,132.4)} = 74.7$, $p < 0.001$	Ref > NDPE > DPE
Friendship Support	CFQ	13.47 (2.4)	13.15 (2.68)	9.75 (3.76)	$F_{(2,120.8)} = 28.3$, $p < 0.001$	Ref = NDPE, Ref > DPE, NDPE > DPE
In Full-Time Education	Self-Report	68.90%	56.90%	69.20%	$\chi^2 = 5.4$, DF = 2, p = 0.273	-
In Full-Time Employment	Self-Report	0.30%	0%	1.50%	$\chi^2 = 2.6$, DF = 2, p = 0.474	-
Unemployed	Self-Report	0.30%	1.90%	0%	$\chi^2 = 4.2$, DF = 2, p = 0.374	-

Table 7.5: Follow-up comparisons of Reference, NDPE and DPE cluster in NSPN 17-19

Variable	Instrument	Reference	NDPE	DPE	Omnibus	Pairwise Comparisons
Male	Self-Report	49%	49.10%	37.30%	$\chi^2 = 3.2$, DF = 2, p = 1	-
Non-white Ethnicity	Self-Report	26.50%	45.60%	28.40%	$\chi^2 = 8.7$, DF = 2, p = 0.104	-
Socio-economic Status	IMD	0.02 (1.03)	-0.39 (0.95)	-0.02 (1.01)	$F_{(2,100.9)} = 3.8$, $p = 0.158$	-

Variable	Instrument	Reference	NDPE	DPE	Omnibus	Pairwise Comparisons
Mental Illness in First Degree Relative	Self-Report	7.50%	3.50%	16.40%	$\chi^2 = 7.8$, DF = 2, p = 0.139	-
Cannabis Use	Self-Report	14.70%	14%	19.40%	$\chi^2 = 1$, DF = 2, p = 1	-
Lifetime Help-Seeking for Mental Illness	Self-Report	6.10%	3.50%	31.30%	$\chi^2 = 45$, DF = 2, p < 0.001	Ref = NDPE, Ref < DPE, NDPE < DPE
Current Help-Seeking for Mental Illness	Self-Report	2.30%	0%	21.20%	$\chi^2 = 47.3$, DF = 2, p < 0.001	Ref = NDPE, Ref < DPE, NDPE < DPE
Depressive Symptoms	SMFQ	3.57 (2.11)	6.36 (2.73)	17.53 (4.3)	$F_{(2,83.7)} = 313.8$, p < 0.001	Ref < NDPE < DPE
Anxiety Symptoms	RCMAS	10.43 (6.79)	19.33 (9.75)	38.87 (8.6)	$F_{(2,85.9)} = 306.4$, p < 0.001	Ref < NDPE < DPE
Wellbeing	WEMWBS-14	45.68 (6.64)	41.4 (7.58)	31.39 (8.26)	$F_{(2,91.4)} = 102.8$, p < 0.001	Ref > NDPE > DPE
Asociality	SPQ	3.22 (3.32)	7 (4.46)	11.09 (4.6)	$F_{(2,83)} = 86.6$, p < 0.001	Ref < NDPE < DPE
Social Anxiety	SPQ	3.03 (2.37)	4.13 (2.3)	6.39 (1.81)	$F_{(2,102.4)} = 74.5$, p < 0.001	Ref < NDPE < DPE
Eccentricity	SPQ	1.4 (1.94)	3.59 (2.54)	5.19 (2.27)	$F_{(2,83.8)} = 79.2$, p < 0.001	Ref < NDPE < DPE
Odd Speech	SPQ	2.01 (1.67)	3.72 (1.54)	4.41 (1.57)	$F_{(2,99.4)} = 70$, p < 0.001	Ref < NDPE < DPE
Childhood Adversities	MOPS	7.14 (7.56)	12.82 (9.41)	22.31 (15.38)	$F_{(2,71.2)} = 33.3$, p < 0.001	Ref < NDPE < DPE

Variable	Instrument	Reference	NDPE	DPE	Omnibus	Pairwise Comparisons
Family Support	FAD	37.87 (5.96)	35.58 (6.68)	29.07 (7.68)	$F_{(2,93.2)} = 37.1$, $p < 0.001$	Ref > NDPE > DPE
Friendship Support	CFQ	13.62 (2.57)	12.45 (2.84)	9.76 (3.9)	$F_{(2,85.4)} = 27.9$, $p < 0.001$	Ref > NDPE > DPE
In Full-Time Education	Self-Report	75.20%	75.40%	71.40%	$\chi^2 = 0.4$, DF = 2, p = 1	-
In Full-Time Employment	Self-Report	6.50%	5.30%	7.90%	$\chi^2 = 0.4$, DF = 2, p = 1	-
Unemployed	Self-Report	3.50%	3.50%	6%	$\chi^2 = 1$, DF = 2, p = 1	-

Table 7.6: Follow-up comparisons of Reference, NDPE and DPE cluster in NSPN 20-25

Variable	Instrument	Reference	NDPE	DPE	Omnibus	Pairwise Comparisons
Male	Self-Report	48.10%	52%	47.60%	$\chi^2 = 0.6$, DF = 2, p = 0.728	-
Non-white Ethnicity	Self-Report	15.80%	28.50%	14.30%	$\chi^2 = 10.9$, DF = 2, p = 0.025	Ref < NDPE, Ref = DPE, NDPE = DPE
Socio-economic Status	IMD	0.11 (0.96)	-0.13 (0.93)	-0.25 (0.88)	$F_{(2,92)} = 4.6$, $p = 0.052$	-
Mental Illness in First Degree Relative	Self-Report	9.40%	9.80%	40.50%	$\chi^2 = 36.9$, DF = 2, p < 0.001	Ref = NDPE, Ref < DPE, NDPE < DPE
Cannabis Use	Self-Report	11.80%	11.40%	28.60%	$\chi^2 = 10$, DF = 2, p = 0.033	Ref = NDPE, Ref < DPE, NDPE < DPE

Variable	Instrument	Reference	NDPE	DPE	Omnibus	Pairwise Comparisons
Lifetime Help-Seeking for Mental Illness	Self-Report	11.10%	21.10%	64.30%	$\chi^2 = 81$, DF = 2, p < 0.001	Ref < NDPE < DPE
Current Help-Seeking for Mental Illness	Self-Report	2.60%	6.60%	47.60%	$\chi^2 = 131.7$, DF = 2, p < 0.001	Ref < NDPE < DPE
Depressive Symptoms	SMFQ	3.21 (1.96)	8.29 (3.05)	19.74 (4.15)	$F_{(2,79.6)} = 401.4$, p < 0.001	Ref < NDPE < DPE
Anxiety Symptoms	RCMAS	9.4 (6.94)	21.78 (9.11)	42.03 (7.76)	$F_{(2,85)} = 370.9$, p < 0.001	Ref < NDPE < DPE
Wellbeing	WEMWBS-14	45.94 (6.24)	39.86 (6.5)	28.89 (7.57)	$F_{(2,88.1)} = 135$, p < 0.001	Ref > NDPE > DPE
Asociality	SPQ	2.47 (3.29)	7.25 (4.01)	10.14 (4.32)	$F_{(2,79.4)} = 117.6$, p < 0.001	Ref < NDPE < DPE
Social Anxiety	SPQ	2.76 (2.21)	4.33 (2.55)	6.35 (2.25)	$F_{(2,85.7)} = 51.4$, p < 0.001	Ref < NDPE < DPE
Eccentricity	SPQ	1.22 (1.9)	4.08 (2.55)	5.33 (2.5)	$F_{(2,78.2)} = 87$, p < 0.001	Ref < NDPE < DPE
Odd Speech	SPQ	1.71 (1.67)	3.64 (1.64)	4.24 (1.68)	$F_{(2,87.2)} = 81.9$, p < 0.001	Ref < NDPE, Ref < DPE, NDPE < DPE (trend)
Childhood Adversities	MOPS	6.68 (8.5)	14.83 (12.44)	22.57 (18.01)	$F_{(2,72.1)} = 37$, p < 0.001	Ref < NDPE < DPE
Family Support	FAD	38.88 (5.93)	33.89 (6.75)	30.54 (8.06)	$F_{(2,83.1)} = 42$, p < 0.001	Ref > NDPE > DPE
Friendship Support	CFQ	13.72 (2.69)	11.78 (3.04)	8.11 (3.88)	$F_{(2,82.3)} = 52.7$, p < 0.001	Ref > NDPE > DPE

Variable	Instrument	Reference	NDPE	DPE	Omnibus	Pairwise Comparisons
In Full-Time Education	Self-Report	49.70%	43.90%	28.60%	$\chi^2 = 7.5$, DF = 2, p = 0.069	-
In Full-Time Employment	Self-Report	35.80%	30.10%	23.80%	$\chi^2 = 3.4$, DF = 2, p = 0.36	-
Unemployed	Self-Report	3.80%	10.60%	28.60%	$\chi^2 = 40.7$, DF = 2, p < 0.001	Ref < NDPE < DPE

See Tables 7.3 and 7.4 - 7.6 for comparisons of Reference, NDPE and DPE in ROOTS and NSPN 14-16, 17-19 and 20-25 respectively.

Sociodemographic characteristics, family mental illness and cannabis use

In ROOTS, NDPE and DPE showed no sociodemographic differences. Compared to Reference, NDPE and DPE were less likely to be male and more likely to have a family history of mental illness; NDPE showed a trend towards increased cannabis use.

In NSPN, at ages 14-16, NDPE and DPE were more likely to be of non-white ethnicity and have lower socioeconomic status than Reference. These differences were not clearly replicated in the older age groups. In those aged 20-25 and at trend-level in those aged 17-19, NDPE and Reference were less likely than DPE to have mental illness in a first degree relative.

PE characteristics

In ROOTS, NDPE showed some increase in all symptoms compared to Reference, but showed only a trend-level decrease in wellbeing. Notably, 21.3% of NDPE had a current mental disorder at 17, compared to 6.5% of Ref and 52.8% of DPE. This suggests that PEs without distress still confer some risk of mental illness but confirms that some PEs are associated with far greater risk than others. DPE had higher symptoms of anxiety and lower wellbeing compared to Reference and DPE in all domains, suggesting this cluster is not psychosis-specific but shows transdiagnostic markers of psychopathology.

Similar patterns were found in NSPN that became more pronounced as age increased. DPE had higher lifetime and current help-seeking than Reference and NDPE in all age groups. NDPE showed higher rates of current and lifetime help-seeking than Reference in those aged 20-25 only, with a trend-level increase in current help-seeking in those aged 14-16.

Current and past symptoms and current mental disorders or help-seeking for mental illness

In ROOTS, NDPE showed some increase in all symptoms compared to Reference, but showed only a trend-level decrease in wellbeing. Notably, 21.3% of NDPE had a current mental disorder at 17, compared to 6.5% of Ref and 52.8% of DPE. This suggests that PEs without distress still confer some risk of mental illness but confirms that some PEs are associated with far greater risk than others. DPE had higher symptoms of anxiety and lower wellbeing compared to Reference and DPE in all domains, suggesting this cluster is not psychosis-specific but shows transdiagnostic markers of psychopathology.

Similar patterns were found in NSPN that became more pronounced as age increased. DPE had higher lifetime and current help-seeking than Reference and NDPE in all age groups. NDPE showed higher rates of current and lifetime help-seeking than Reference in those aged 20-25 only, with a trend-level increase in current help-seeking in those aged 14-16.

Childhood adversity and recent social support

In ROOTS, DPE and NDPE were similarly exposed to childhood adversity and were more exposed to childhood adversity than Reference, supporting that early-life trauma may generally predispose to psychotic phenomena. In contrast, Reference and NDPE showed similar levels of social support from family and friends at ages 14 and 17, and far higher levels of support than DPE.

In NSPN, DPE experienced more childhood adversity than NDPE, who experienced more adversity than Reference. This difference may be explained by the use of a self-report retrospective measurement made at the same time of clustering, rather than a caregiver-report instrument made earlier. The patterns of high levels of social support in Reference and NDPE but not DPE were replicated in all samples.

Education and employment

There was little evidence of educational impairment in ROOTS, with no differences in secondary school qualifications across the clusters.

In NSPN, differences only emerged in the age 20-25 sample. DPE were more likely to be unemployed than NDPE, who were more likely to be unemployed than Reference, suggesting increasing functional impairment.

Schizotypal traits (NSPN)

Schizotypal traits of asociality, social anxiety, eccentricity and odd speech increased from Reference to NDPE to DPE (trend-level for NDPE $<$ DPE for odd speech), suggesting increasing proneness to psychosis-associated traits. However, the psychosis-specificity of this pattern should be interpreted cautiously given the transdiagnostic symptom profile of the DPE clusters.

7.4.6 Similarity of cluster profiles across adolescence and early adulthood

Figure 7.6: Cross-classification of participants in different age bins in NSPN

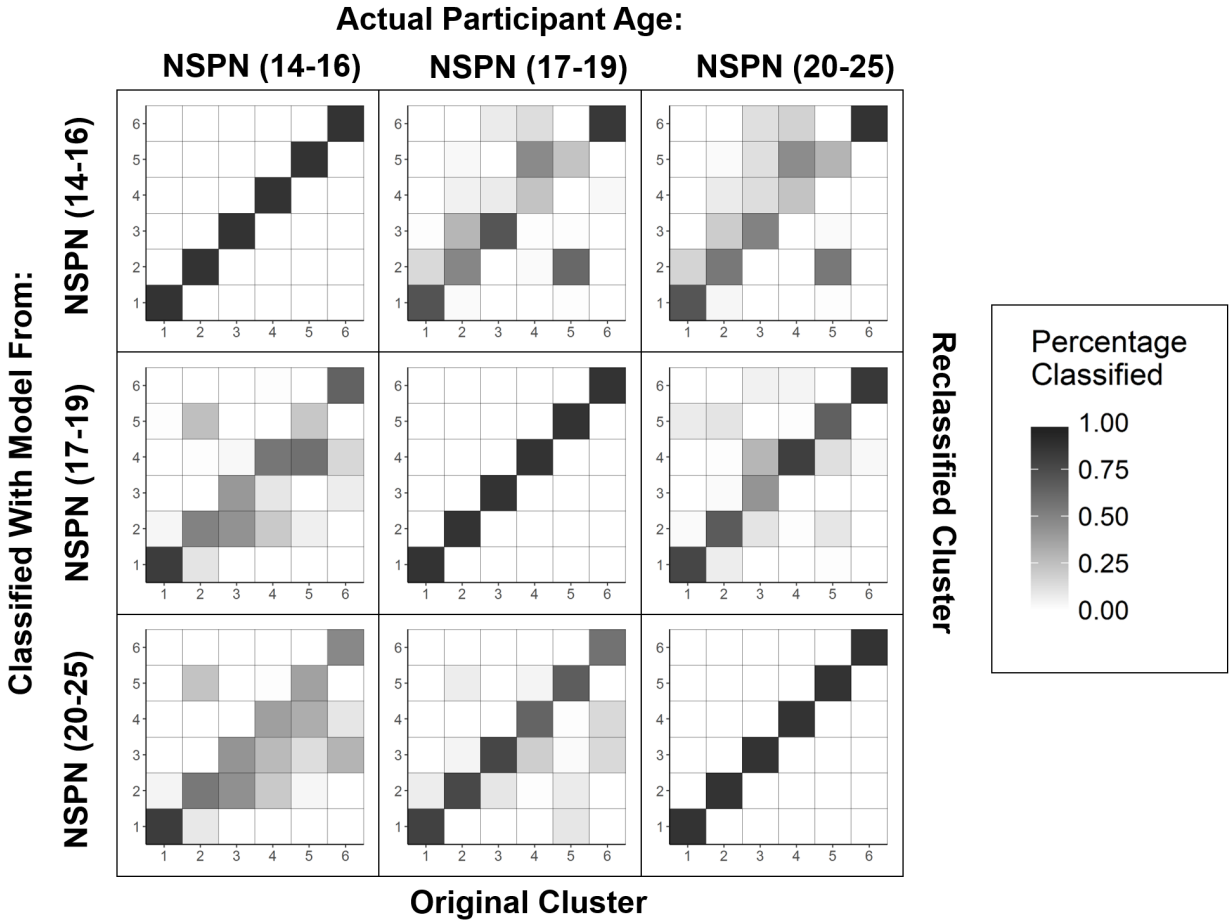


Figure 7.6: To compare similarity of clustering solutions across age, participants in each age bin were re-classified according to the models for the other age bins. The clustering models for ages 17-19 and 20-25 are fairly similar to one another, while the model for ages 14-16 appears more distinct. There may be distinct patterns of psychotic phenomena and distress that change through late adolescence and early adulthood.

When cross-classified according to the latent class probabilities of the other age groups, there was greater similarity between the 17-19 and 20-25 age groups than for 14-16 and the other groups, despite the similar symptom profiles and convergent results found for most comparisons (Figure 7.6). This suggests that psychotic phenomena and depressive symptoms may show slightly different manifestations in younger adolescents than older adolescents and young adults. In particular, NDPE was larger in age 14-16 than the other age groups and around half of the participants were reclassified as NDPE and half as cluster 2 (low scores on all symptoms) according to the older age models. Similarly, DPE was larger in age 14-16 than the other age groups and only 74% and 55% of 14-16 DPE reclassified as DPE by the 17-19 and 20-25 models, respectively. In contrast, 97% and 100% of age 17-19 and 20-25 DPE, respectively, were reclassified as DPE by the age 14-16 model.

7.5 Discussion

In this chapter, I found evidence that PEs manifested in clusters of young people with extremely high levels of distress ('distressed & PE-prone', DPE) and without high levels of distress ('non-distressed & PE-prone', NDPE) in two cohorts of young people, with one cohort divided into three age bins and analysed independently. When compared to one another and a 'Reference' cluster without PEs or distress, I found replicable patterns of associations with types of PEs, other mental health symptoms, diagnoses & help-seeking for mental disorders, childhood adversity and social support. Importantly, the NDPE phenotype did not appear to be a measurement artefact or mild psychosis-proneness, with similar levels of interview-verified PEs, including those persisting for at least a year, in the DPE and NDPE groups.

These results clearly demonstrate that PEs are not necessarily a symptom of psychopathology and that nonclinical PEs are not simply an attenuated form of psychosis-proneness, a measurement artefact or a highly unusual phenotype that could not be identified in representative samples. Nonetheless, convergent results from Appendix C and this chapter support that PEs are a manifestation of extreme distress and that people experiencing the highest levels of distress were highly likely to experience PEs, as well as being at high risk of other symptoms and of common, nonpsychotic mental disorders and social dysfunction. These findings support recent shifts in psychosis high-risk research away from focusing solely on positive symptoms and towards integrating measurements of positive symptoms with social dysfunction and cognitive impairment (Fusar-Poli et al., 2014b). The clustering results also suggest there may be unmet health needs in 14-16 year olds, identifiable by self-report symptom measurements.

These findings suggest a number of environmental factors that might either reflect or modify health and psychosis-proneness trajectories that warrant further investigation. In particular, childhood adversity and social dispositions/social support appear to have dissociable relationships with health outcomes. Social support from friends and family should be investigated as either a predictor or modifiable environmental influence on future health in young people prone to PEs.

Future work will require investigating the longitudinal pathways to PEs with and without distress. Studies that are better equipped to establish causative relationships, like randomised controlled trials or Mendelian randomization paradigms could help shed light on whether differences in social support are symptomatic or causative. Finally, it is necessary to move beyond the level of symptom description to computational and implementational mechanisms of PEs, which may help establish whether PEs with and without distress represent the same or fundamentally different phenomena.

7.5.1 Sociodemographic factors

There were not replicable sociodemographic factors that differentiated the groups. Some observed differences, such as increased family history of mental illness and lower socioeconomic status in the psychosis-prone groups were expected but the lack of clear association with cannabis use was surprising. This may be in part due to the measurement of only recent cannabis use, in the

month prior to assessment.

7.5.2 Types of PEs

NDPE and DPE had similar levels of interview-verified PEs overall and of hallucinations and anomalous experiences when types of PE were examined separately. These groups were just as likely to have PEs that had persisted for at least a year and to have PEs occurring in the last year. Around 17% of both NDPE and DPE had PEs persisting for at least a year, meaning I can roughly estimate the population prevalence of non-distressed and distressed adolescents with persistent PEs at 1.6% and 0.9%, respectively, suggesting that these phenotypes occur with non-negligible frequencies. Consistent with previous findings (Lovatt et al., 2010; Brett et al., 2014; Ward et al., 2014), delusions and paranoid ideation were more associated with distress than hallucinations, anomalous experiences, unusual perceptions and non-paranoid unusual beliefs. These results suggest that it may not be the occurrence, intensity or even persistence of PEs that determine clinical relevance as much as a person's appraisals of them and the extent to which those PEs reflect distorted, threatening beliefs about the world.

7.5.3 Symptoms, diagnoses and help-seeking for mental illness

Unsurprisingly, the DPE group had very high rates of nonpsychotic mental disorders, particularly current mental disorders and multiple comorbid disorders over the lifetime. DPE was reliably associated with lower wellbeing and symptoms of anxiety. DPE was also associated with help-seeking for mental illness in all NSPN age groups, particularly in the young adults. These results support that PEs are not a specific feature indicating psychosis risk, but are a transdiagnostic feature indicating severe distress and general risk of mental illness. The instruments used did not allow me to measure whether people are distressed by their PEs, or whether PEs are non-distressing but incidental to high levels of depressive symptoms. This may be a critical feature in distinguishing people who may be at high-risk for psychotic disorders from those who are at higher risk of other illnesses like affective disorders.

In ROOTS, the NDPE group had higher rates of mental disorders than expected, with just over half meeting or having high clinical index of mental illness at some point in their lifetime. The greater lifetime prevalence than current prevalence and prevalence 3 years prior to clustering suggest that this group may be at risk of psychopathology at younger ages but could represent a 'recovered' group at age 17. NDPE and DPE did appear more similar in terms of current mental disorders and depressive symptoms at age 14 in ROOTS and it is possible that the NDPE and DPE groups diverge later in adolescence. If this is true, a critical point that remains unknown is whether, at earlier ages, these groups form a common pool of psychosis-prone young people with trajectories that are not fixed and may still differentiate into good or ill health outcomes based on other factors, or whether those who go on to manifest as distressed and non-distressed are already distinct and committed to a certain phenotype but without full manifestation of their symptoms. If these trajectories are not fixed, identifying the determinant risk and protective factors may enable targeted interventions with the goal of primary prevention. If the trajectories are fixed, it may require looking earlier in development to identify the factors that determine

later psychopathology and impairment.

The lower rates of help-seeking in NSPN in those aged 14-16, despite similarly high levels of depressive and paranoid symptoms in DPE at all age ranges, may indicate unmet healthcare needs in younger adolescents. Barriers to adequate healthcare may be stigma against mental illness, poorer availability of health care or inadequate recognition of clinically-relevant symptoms in this age range.

7.5.4 Childhood adversity

Both NDPE and DPE were associated with childhood adversity, replicating evidence that trauma in early life predisposes to both clinical and nonclinical PEs (Bebbington et al., 2004; Arseneault et al., 2011; Daalman et al., 2012; Varese et al., 2012). Self-report parent-focused adversities were greater in DPE than NDPE in all NSPN age groups, but NDPE and DPE had similar exposure to adversities measured using a detailed interview with caregivers at an earlier time point. A possible difference between these measures is that retrospective measurements may capture some of a person's response to and appraisals of trauma, such as through biased recall of highly impactful events or forgetting of events with little impact, supported perhaps by evidence of under-recall of adversities using self-report measurements (Hardt and Rutter, 2004). If true, the results suggest that exposure to adversities predisposes to PEs but exposure to highly impactful adversities with negative appraisals tends also towards severe symptoms of distress. However, there is evidence that retrospective measures of adversity are reliable and not affected by symptom load in psychosis (Fisher et al., 2011), post-traumatic stress disorder (Goodman et al., 1999) or depression (Brewin et al., 1993; Gerlsma et al., 1993). Understanding the pathways from childhood adversities to clinical and nonclinical PEs is likely to require more detailed measurements of adversities and appraisals of them and may be aided by investigation of potential mediating factors like dissociation and negative affect (Hardy et al., 2016).

7.5.5 Social support

Social support from family and friends was markedly lower in the DPE group than the Reference group in all samples at time of clustering and 3 years prior to clustering in ROOTS. In contrast, NDPE showed either similar or slightly lower levels of support compared to Reference and greater support than DPE at time of clustering in all samples. In ROOTS, NDPE had greater family support than DPE 3 years prior to clustering but similar levels of friendship support. These replicable differences in social support suggest that it may be a critical feature distinguishing people with PEs with and without concurrent distress. Social support comprises social networks, 'enacted' support that is actually provided in times of stress and 'perceived' support of how supported a person feels by social relationships.

Explanations for this relationship can broadly be defined in two, not mutually-exclusive ways. The relationship may be 'symptomatic', in that whatever psychopathology tends towards PEs and distress also tends towards impaired social functioning that makes it difficult to maintain positive relationships with peers and family members. Consistent with this, psychotic illness is associated with poor social support, both in chronic (Beels, 1981; Buchanan, 1995; Meesters et

al., 2010) and early disease stages (Gayer-Anderson and Morgan, 2013). Poor premorbid levels of functioning and social integration predict later psychosis (Malmberg et al., 1998; Cannon et al., 2008; Velthorst et al., 2009; Dragt et al., 2011), with progressive impairment leading up to onset of psychotic disorder (Velthorst et al., 2016).

The relationship may also be 'causative', in that good social support protects against distress while poor support predisposes to it. Social support is thought to be a critical component of resilience to stress (Cohen and Wills, 1985) and could interact with the proposed psychosis-promoting mechanisms of adversity. Supportive relationships through friends, family or other social environments may promote the normalisation and adaptive appraisal of aberrant experiences (Claridge, 1997; Farias et al., 2013; Peters et al., 2016), tend away from negative schema (Brown et al., 1986) and negative affect (Powers et al., 2009), reduce the stress that aberrant experiences cause (Brett et al., 2014) and act as a general buffer against stress from all causes. Importantly, social support may be modifiable and boosting support in people at risk of disorder or in their early stages might shift some young people towards the non-distressed, versus the distressed phenotype. Clinical trials of support-based interventions are rare, but promising family and friendship-based interventions have shown some success at preventing relapse and minimising symptoms of psychotic illness (McFarlane et al., 2003; O'Brien et al., 2014; Poulton et al., 2014; Harrop et al., 2015).

7.5.6 Functional impairment

Clear evidence of impairment in education or employment was only found in young adults in NSPN, in whom unemployment was higher in DPE than NDPE and in NDPE than in Reference. This may be that the measurements of proportions in education, training and the numbers of secondary school qualifications are not sensitive enough to pick up differences in functioning in younger people. For example, unemployment is unlikely to be a meaningful variable in 14-16 year olds.

7.5.7 Age differences

In NSPN, the clustering models for 17-19 and 20-25 year olds were more similar to one another than they were to the model for 14-16 year olds, evidenced by the high cross-classification accuracy in the older groups. This suggests that, while very similar symptom profiles were found across ages, the exact nature of these profiles differs in younger adolescents versus older adolescents and young adults.

7.5.8 Strengths & limitations

This study has a number of strengths. The greatest strength is replication of key findings across two cohorts, one representative and one near-representative but balanced for age and sex. Very similar symptom clusters were identified in four separate data-driven analyses with data collected using only partially-overlapping instruments, centres and ages. A number of key factors reliably

distinguished key clusters of interest and a number of these support previous findings obtained in highly-selected samples.

This study also has limitations. Some clusters were not considered in detail and some clusters were not as clearly replicated across all groups. The use of a 'classify-analyse' approach risked attenuating relationships between clusters and other variables. The use of mainly self-report measurement to perform latent class clustering may have introduced measurement error, though I showed in Chapter 5 that the PLIKSi and BSSI measure the same underlying phenomena.

7.6 Future questions

Based on the results of the previous chapters, I selected a set of questions that could feasibly be investigated in ROOTS or NSPN or in novel datasets, based around understanding longitudinal development of PEs and their computational mechanisms and focusing particularly on the relationships between PEs and the social environment.

7.6.1 How do PEs and social dispositions/social relationships influence one another over time?

Social support and social functioning may be critical determinants of health in people with PEs. This may be because PEs cause or precede social dysfunction or social dysfunction causes or precedes PEs. Poor social networks are a risk factor for developing psychosis and disruptions to social networks, social interactions and societal functioning often precede the onset of PEs (Jones et al., 1994; Velthorst et al., 2012, 2016; Gayer-Anderson and Morgan, 2013). Collip et al. (2013) (Collip et al., 2013) showed that interpersonal difficulties in relationships with family and friends consistently predicted bizarre experiences and paranoid ideation in a general population sample of adolescents, though with important methodological limitations (see next chapter). I planned to investigate possible bidirectional longitudinal associations between social difficulties and dimensions of PEs in NSPN using cross-lagged structural equation modelling, controlling measurement invariance and covariates and testing whether any effects are mediated by influences on real-world social support from friends and family.

7.6.2 How are childhood adversity and social support related to one another and to later manifestation of distress and PEs?

Childhood adversity and social support later in life are rarely considered together in relation to psychosis (Gayer-Anderson et al., 2015), though both are associated with it (Varese et al., 2012; Gayer-Anderson and Morgan, 2013). My results, like others, support that childhood adversity may predispose to both clinically-relevant and nonclinical PEs (Lovatt et al., 2010; Daalman et al., 2012), while social support, which may be a proxy of social functioning and negative symptoms, strongly separates them (Sommer et al., 2010; Peters et al., 2016). Two important questions are how adversity and support relate to one another and how important social relationships at different stages of development are for later PEs and distress. I planned to investigate these questions using longitudinal data from both NSPN and ROOTS.

Chapter 8

Asociality increases positive psychotic phenomena in adolescents and young adults by worsening social relationships

Abstract

Social difficulties are associated with psychotic experiences and may precede and contribute to development of psychosis. Using cross-lagged structural equation modelling in NSPN, I investigated bidirectional, longitudinal interactions over 12 months between asocial dispositions (ASO) and two dimensions of positive psychotic phenomena (anomalous experiences and beliefs, AEB; paranoid ideation, PI). These were measured by a novel factorial structure of the Schizotypal Personality Questionnaire that out-competed existing structures on thorough psychometric validation and were invariant over time. I investigated whether these relationships were mediated by impairing social relationships and whether ASO, AEB and PI predict later markers of psychopathology. ASO, AEB and PI are relatively stable over 12 months. ASO predicted future AEB and PI, while neither AEB nor PI predicted future ASO, suggesting withdrawal from social interaction precedes or promotes psychotic phenomena. The effects of ASO predicting AEB and PI were fully mediated independently by detriment to family relationships and friendships. ASO and PI predicted depressive symptoms and ASO alone predicted psychiatric help-seeking. The social environment may be important in predicting or modifying psychosis and psychopathology. Poor social relationships may promote psychosis indirectly by reducing stress-resilience and directly by impairing use of socially-derived information to shape perception and belief updating.

8.1 Research Questions

- How do PEs and social dispositions/social relationships influence one another over time?

8.2 Introduction

While psychosis is characterised according to the presence of delusions and hallucinations, it typically involves impairment of social function and withdrawal from social interaction. Moreover, poor social networks are a risk factor for developing psychosis and disruptions to social networks, social interactions and societal functioning often precede its onset (Jones et al., 1994; Velthorst et al., 2012, 2016; Gayer-Anderson and Morgan, 2013).

Similarly, when psychosis-like phenomena occur in the general population as 'schizotypal' personality (Meehl, 1962; Claridge and Beech, 1995) or an 'extended psychosis phenotype' (van Os et al., 2009; van Os and Reininghaus, 2016), social difficulties are common and predict poor functioning, later subclinical positive psychotic phenomena and clinical psychosis (Dominguez et al., 2010; Collip et al., 2013). Standardized instruments capture this as 'interpersonal' schizotypy, characterised by social anhedonia, lack of close relationships and social anxiety (Raine et al., 1994).

Given these findings, interpersonal difficulties could have a causal role in the development of psychotic experiences (PEs) or influence health outcomes in people prone to them. Social relationships might influence PEs through various mechanisms. One possibility is that a lack of social support could exacerbate the effects of stress (Zubin and Spring, 1977; Nuechterlein and Dawson, 1984). Another is that social involvement and interactions are important information sources that shape our experience of and inferences about the world. We learn vicariously in uncertain environments (Toelch et al., 2014) and find value in conforming to the beliefs of others (Campbell-Meiklejohn et al., 2012), which may provide a crucial component of our evaluation of external reality. Atypical use of socially-derived information, such as poor learning or use of information from other people in decision making (Cook et al., 2014) or perceptual inference (Mahmoodi et al., 2013; Hertz et al., 2016), might impair a person's ability to accurately learn and predict properties of the environment and other agents, leading to experiences and beliefs that deviate from social norms. Such a proposal has direct links with current computational models of the emergence of psychotic experiences. These posit that reality distortion can be described by false inferences (such as wrongly inferring the causes of sensory inputs, leading to hallucinations) and false updating of internal models or prior knowledge (leading to aberrant beliefs about the world, or delusions) (Fletcher and Frith, 2009; Corlett et al., 2010; Adams et al., 2013). Both inappropriate inferences and inappropriate model updating might arise from atypical integration of prior knowledge with sensory information, a process that depends critically on the computation and signalling of prediction errors and that guides perception, action and decision making (Friston, 2005; Den Ouden et al., 2012).

In this study, I sought to explore the relationship between social dispositions and psychosis-proneness by determining whether interpersonal difficulties promote positive psychotic phenomena over 12 months in a general population sample of adolescents and young adults. I further sought to determine whether such effects are mediated by changes in quality of friendships or family relationships. Finally, I compared how different dimensions of the extended psychosis phenotype are associated with future psychopathology, indexed by psychiatric help-seeking and depressive symptoms.

I used cross-lagged structural equation modelling (SEM) to test whether either social difficulties or positive psychotic phenomena predict themselves ('autoregressive' effects) and each other ('cross-lagged' effects) in the future, taking baseline levels and covariance at both times into account. I used strict modelling constraints to ensure I was measuring the same latent constructs at different time points (longitudinal measurement invariance).

Collip et al. (2013) showed, using methodologically-similar cross-lagged path analysis, that interpersonal difficulties in relationships with family and friends consistently predicted bizarre experiences and paranoid ideation in a general population sample of adolescents. I replicate and extend their findings in a larger sample ensuring measurement invariance over time, minimising measurement error by estimating latent variables, thoroughly controlling for covariates and investigating mediation by effects on actual social relationships and social support.

I evaluated the following hypotheses: positive psychotic phenomena and interpersonal difficulties will be largely stable over 12 months, evidenced by significant autoregressive effects; interpersonal difficulties at baseline will be informative of positive psychotic phenomena at 12-month follow up, evidenced by significant cross-lagged effects; cross-lagged effects will be mediated by baseline social difficulties impairing quality of friendships or family relationships at 12-month follow-up; interpersonal difficulties will be the best predictor, compared to positive psychotic phenomena, of future depressive symptoms and psychiatric help-seeking or diagnosis.

8.3 Methods

8.3.1 Data

Data came from the NSPN 2400 cohort. For full information on the NSPN cohort, see Methodology.

8.3.2 Schizotypal Personality Questionnaire (SPQ)

The Schizotypal Personality Questionnaire (Raine, 1991) is a self-report questionnaire comprising 74 true-or-false statements with 9 subscales designed to measure the domains of schizotypal personality disorder, as of DSM-III (Association, 2013).

These 9 subscales are often summarised by usually 3 (Raine et al., 1994) or 4 (Stefanis et al., 2004) higher-order factors. However, both the 9 subscales and the higher-order factors may fit item-level data poorly (Chmielewski and Watson, 2008). In Chapter 6, I showed that 6 factors can explain item-level responses on the SPQ and outperform the current 3-factor, 4-factor and 9-subscale models.

The 6-factor model provides broad measurements of two dimensions of reality distortion and one of social difficulties, which were the main focus of this study. 'Anomalous experiences & beliefs' (AEB) measures unusual perceptual experiences and magical thinking. 'Paranoid ideation' (PI) measures unusual ideas about connections with other people and others intentions to harm you. 'Asociality' (ASO) is a dimension comprising social difficulties, lack of close relationships and

social anhedonia. Also measured are 'Eccentricity', 'Social Anxiety' and 'Odd Speech'. These dimensions are not considered in this study.

8.3.3 Social support

Social support from peers was measured using the Friendship Quality scale of the Cambridge Friendships Questionnaire (Memarzia et al., n.d.; Goodyer et al., 1989) (CFQ), which comprised 5 self-report Likert-scale items. Social support from family and family functioning was measured with the Family Assessment Device – General Functioning scale (Epstein and Baldwin, 1983) (FAD), which comprised 12 self-report Likert-scale items. Instrument scores were centred and scaled to unit variance.

8.3.4 Cross-lagged structural equation models

In cross-lagged models, the same latent variables are estimated at multiple time points and linked by regression paths measuring a form of residualised population-level change. Cross-lagged models contain 'autoregressive' paths of one latent variable to itself at a later time, measuring that variable's stability. They also contain 'cross-lagged' paths from each latent variable at one time to other latent variables at later times. These indicate whether a variable is additionally predictive of another variable, taking baseline levels into account.

A significant cross-lagged path is sometimes considered evidence of a directional causal relationship. However, I approach causality with extreme caution. Cross-lagged models are usually observational rather than interventional and I cannot rule out the influence of unmeasured covariates. Nonetheless, cross-lagged models suggest causality and allow construction of hypotheses that can be tested in interventional designs. I minimised unmeasured influences by adjusting for potential covariates.

8.3.5 Model estimation

SEMs were fit using the *lavaan* (Rosseel, 2012) package in R, supplemented by functions from *semTools* (semTools Contributors, 2016).

Variables like PI and ordinally-measured item responses were expected to be non-normally distributed. All models were therefore fit with a robust maximum-likelihood (MLR) estimator with robust (Huber-White) standard errors and Satorra-Bentler scaled test statistics. Fit was assessed using CFI & TLI (both > 0.9), the RMSEA (< 0.08) and the SRMR (< 0.06). I calculated the RMSEA of the null model (with no associations between variables), because when the null model fits well (RMSEA < 0.158), fit indices based on comparison between the actual model and null model (CFI & TLI) will be too low and less useful (Kenny, n.d.).

Nonsignificant paths were retained in order to minimise empirical model re-specification. I reported unstandardized and standardized path coefficients, their standard errors and their significance based on Wald tests. Differences between regression paths of interest were additionally

tested using the Satorra-Bentler Chi-Squared test, in which a model was estimated with the regression coefficient (β) of the path of interest constrained to be equal to another path coefficient and fit compared to a model in which those coefficients were freely estimated. A significant result, meaning that constraining that path coefficient resulted in poorer model fit, confirmed that two paths were of different sizes.

In previous chapters, I used multiple imputations (MI) with WLSMV estimators, designed for categorical data, to account for missing data. While MI can provide accurate and unbiased estimation of associations and standard errors, it can produce misleading results if, for example, not enough imputations are used, variables relevant to missingness are not included, outcome variables are omitted from the imputation model or transformations are used in analyses that were not include in the imputation model. It is also highly computationally demanding. In contrast, fiML estimation provides equally accurate and unbiased accommodation of missing data patterns, but is far more computationally efficient, is deterministic (gives the same results every time) and has fewer researcher degrees of freedom, being estimated from the data alone. For these reasons, I chose to use full-information MLR estimation for complex SEM investigations in which item thresholds (obtained through WLSMV estimation) are not of interest, as in this and the remaining chapters.

8.3.6 Covariates

I included potential covariates in all models, with regression paths from each covariate to each latent variable or observed structural variable (social support, depressive symptoms, psychiatric help-seeking). The covariates I included were: age at baseline (continuous), male sex (binary), cannabis use reported in the last month at baseline (binary), socioeconomic deprivation (measured by the rank of the England and Wales governmental Index of Multiple Deprivation (IMD), z-scored), urbanicity (measured using the Rural Urban Classification for England & Wales, https://www.gov.uk/government/collections/rural-urban-classification) non-white ethnicity (binary), family history of psychiatric illness (binary) and maternal qualifications (0 = no qualifications, 1 = secondary school qualifications (age 16), 2 = A-level or equivalent (age 18), 3 = undergraduate degree or higher).

8.3.7 Missing Data

I handled missing data by estimating models using full-information maximum-likelihood (fiML). Logistic regressions confirmed that missingness on all variables was predicted by one or more of the covariates (above).

8.3.8 Longitudinal measurement invariance

I tested longitudinal invariance using multiple-group confirmatory factor analysis. Using time as a grouping variable, I fit a series measurement models (single latent variables), with covariates to support fiML missing data estimation, in which I imposed increasingly strict constraints that model parameters must be equal over time. A decrease in CFI of more than 0.01 of a

more-constrained model over a less-constrained model indicates that those parameters (loadings, intercepts or residuals) are not the same over time.

In all cross-lagged models, I aimed to use models as strictly constrained to be equal over time, with equal loadings and intercepts as minimum. I allowed residual covariance between the same items measured at different time points.

8.3.9 Mediation

I estimated models with quality of friendships and family relationships (both present in the each model) as potential mediators. I tested mediation by examining i) whether the direct path from predictor to outcome (e.g. ASO to AEB) is significant with the mediator included and ii) whether there is a significant indirect path from the predictor to the mediator to the outcome (e.g. ASO to poor friendship quality to AEB). When indirect paths were significant, I estimated percentage of total effect attributable to the mediator by dividing the standardized coefficient of the indirect path by that of the total path (Iacobucci, 2012). I could not establish temporal precedence of outcome and social relationship measurements at follow-up, so do not strongly infer causality.

8.4 Results

8.4.1 Data

Table 8.1: Descriptive statistics of covariates, social support from friends and family and psychopathology variables.

Instrument	Variable	N Complete Data	Mean	Standard error	Median	Median Absolute Deviation	Range
Self-Report	Male	2388	0.47	0.5	0	0	1
Self-Report	Socioeconomic deprivation (IMD)	2376	-0.01	1	0.17	1.24	3.31
Self-Report	Cannabis use at baseline	2388	0.12	0.33	0	0	1
Self-Report	Age (years)	2388	19.08	3.01	18.7	3.51	11.06
Self-Report	Non-white ethnicity	2388	0.23	0.42	0	0	1
Self-Report	Any family psychiatric history	2388	0.11	0.31	0	0	1

Table 8.1 – continued from previous page

Instrument	Variable	N Complete Data	Mean	Standard error	Median	Median Absolute Deviation	Range
Self-Report	Urban-Rural Indicator	2376	5.47	0.75	5	0	5
Self-Report	Maternal educational qualifications	2388	1.73	1.11	2	1.48	3
FAD (Follow-up)	Family support	1646	0	1	0	1.16	3.76
CFQ (Follow-up)	Friendship support	1667	0	1	0.09	1.01	4.08
Self-Report	Current psychiatric help-seeking (Baseline)	2370	0.06	0.23	0	0	1
Self-Report	Current psychiatric help-seeking (Follow-up)	1634	0.06	0.23	0	0	1
SMFQ (Baseline)	Depressive symptoms	2322	7.36	5.49	6	4.45	26
SMFQ (Follow-up)	Depressive symptoms	1770	6.77	5.53	5	4.45	26

2388 participants returned questionnaire packs at time 1 (aged 14-25) and 1808 returned questionnaire packs one year later at time 2 (75.7% retention). At baseline, 2106 participants had complete data on all 74 SPQ items and 2352 had missing data on 5 or fewer items. At follow-up, 1546 had complete data on all SPQ items and 1668 had missing data on 5 or fewer items. Descriptive statistics, including number of complete/missing responses on covariates and social support/psychopathology variables used in latent variable modelling, are shown in Table 8.1.

8.4.2 Longitudinal invariance of psychotic phenomena and asociality

See Table 8.2 for results of longitudinal invariance testing. AEB showed invariant factor loadings and intercepts, but not residuals. PI and ASO showed invariant factor loadings, intercepts and residuals. In all cross-lagged models, loadings and intercepts were constrained to be equal over time.

Table 8.2: Longitudinal measurement invariance testing through multiple-group latent variable modelling. Equiv. Structures = no constraints across time. Weak invariance = equal loadings. Strong invariance = equal loadings and intercepts. Strict invariance = equal loadings, intercepts & residuals. Anomalous Experiences & Beliefs, Paranoid Ideation and Asociality all showed at least strong measurement invariance, supporting the use of cross-lagged structural equation modelling to measure the same construct at different times.

Dimension	Equiv. Structures	Weak	ΔCFI Weak	Strong	ΔCFI Strong	Strict	ΔCFI Strict
Anomalous Experiences & Beliefs (AEB)	0.969	0.968	-0.002	0.962	-0.006	0.952	-0.01
Paranoid Ideation (PI)	0.991	0.99	-0.001	0.989	-0.002	0.981	-0.008
Asociality (ASO)	0.99	0.989	-0.001	0.989	0	0.988	-0.001

Table 8.2

8.4.3 The longitudinal interactions of psychotic phenomena and asociality

Figures 8.1a-c show SEM diagrams with model fit, unstandardized and standardized path coefficients and fit indices. See Appendix B for full parameters and results of Wald significance testing. All models showed adequate fit to the data.

AEB, PI and ASO were stable over 12 months in all models, indicated by significant autoregressive paths with large standardized coefficients. In the AEB/ASO model, ASO at baseline predicted higher AEB at follow-up (standardized estimate = 0.05, z = 2.00, p = 0.046), but baseline AEB did not predict follow-up ASO. The cross-lagged path from ASO to AEB was larger than the path from AEB to ASO ($\beta_{\text{AEB-BL -> ASO-FU}} = \beta_{\text{ASO-BL -> AEB-FU}}$: $\Delta\chi^2 = 4.52$, $\Delta\text{DF} = 1$, p = 0.03).

Figure 8.1: Cross-lagged structural equation models of PEs and asociality

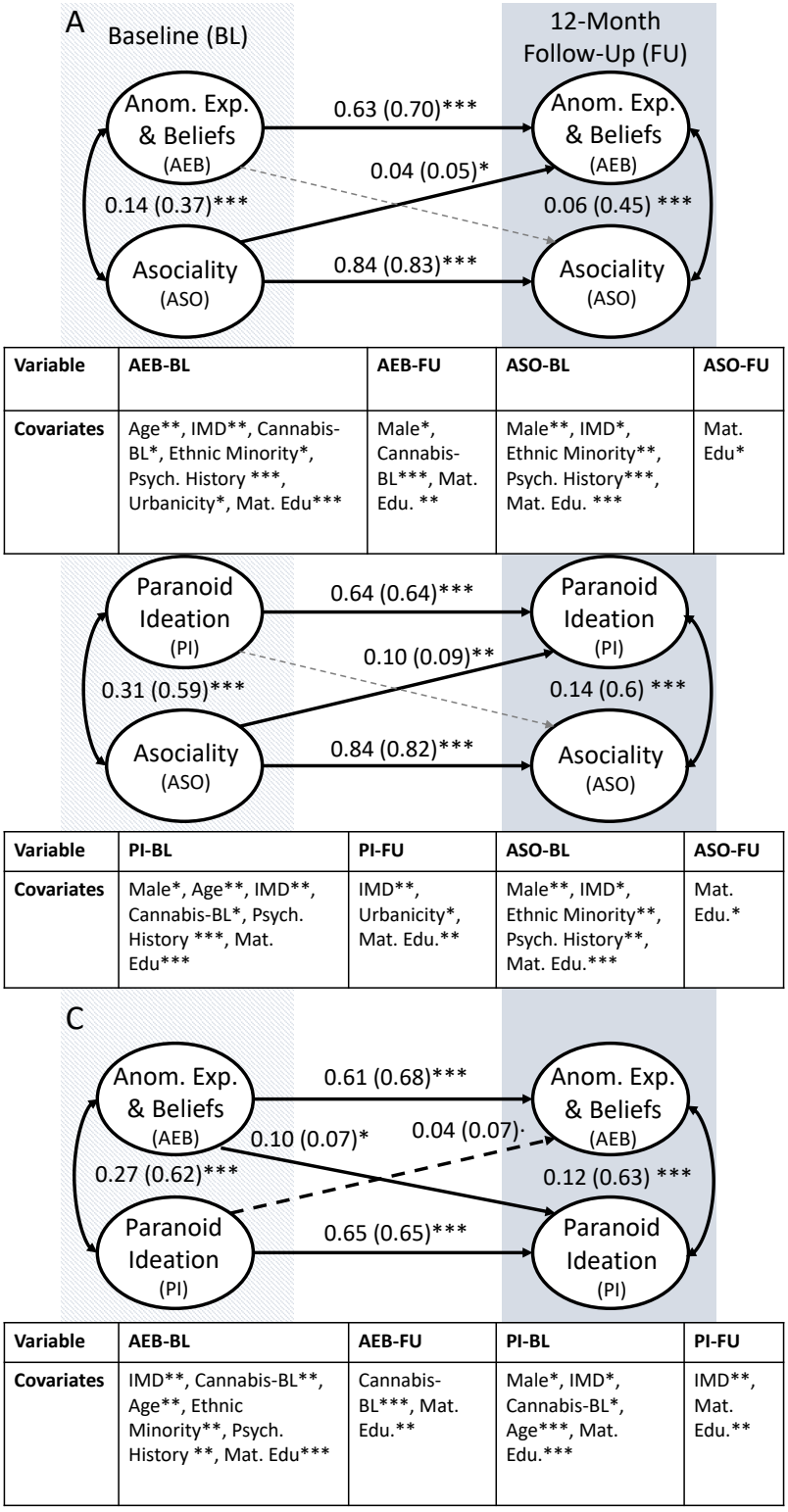


Figure 8.1: Structural equation model diagrams showing cross-lagged effects and significant covariates in final models. Numbers outside of brackets are unstandardized coefficients; standardized coefficients are in brackets. *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$

In the PI/ASO model, baseline ASO predicted higher PI at follow-up (standardized estimate = 0.09, z = 2.92, p = 0.004), but baseline PI did not predict follow-up ASO. The cross-lagged path

from ASO to PI was larger than the path from PI to ASO ($\beta_{\text{PI-BL -> ASO-FU}} = \beta_{\text{ASO-BL -> PI-FU}}$: $\Delta\chi^2 = 6.13$, ΔDF = 1, p = 0.01).

In the PI/AEB model, baseline AEB predicted higher PI at follow-up (standardized estimate = 0.07, z = 2.00, p = 0.045) and baseline PI showed a trend towards higher AEB at follow-up (standardized estimate = 0.07, z = 1.84, p = 0.07). However, the cross-lagged paths from AEB to PI and from PI to AEB did not differ ($\beta_{\text{PI-BL -> AEB-FU}} = \beta_{\text{AEB-BL -> PI-FU}}$: $\Delta\chi^2 = 0.87$, ΔDF = 1, p = 0.87). For this reason, I did not consider the relationships between PI and AEB in mediation analyses.

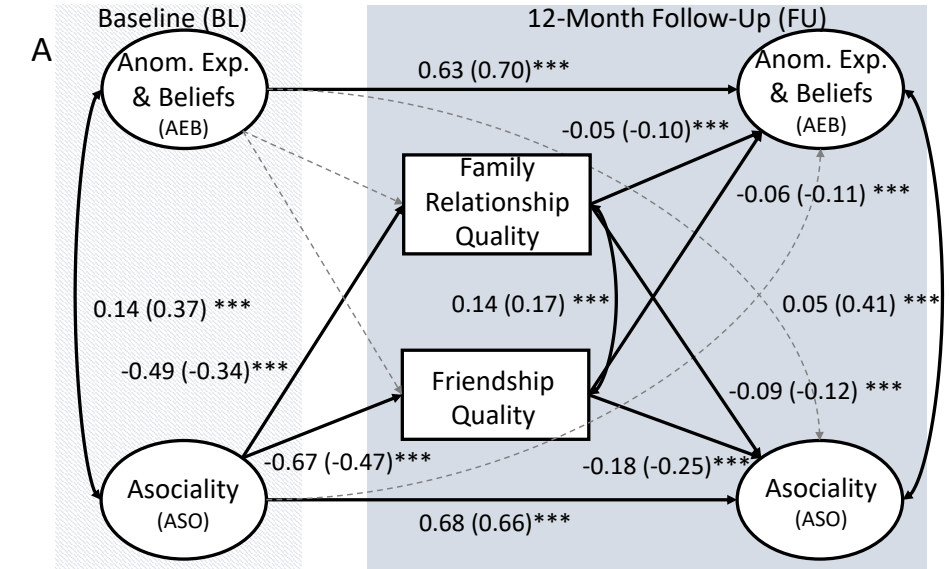
8.4.4 Mediation analysis

Model diagrams of mediation analyses are shown in Figure 8.2A-B. Fit indices for all models exceeded criteria for good fit. Full model parameter estimates and results of Wald significance tests are given in Appendix B.

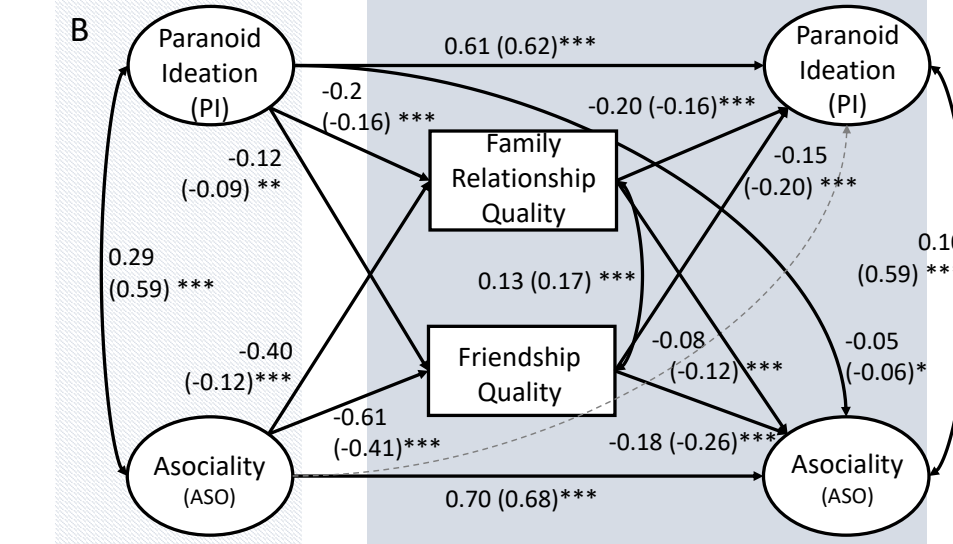
The associations between ASO and follow-up AEB and PI were fully mediated by ASO impairing friendships and family relationships. This was indicated by no remaining significant direct ASO -> AEB or ASO -> PI paths and significant indirect paths via the social relationship variables.

Of the total ASO -> AEB effect, 76.3% was explained by ASO impairing friendships and 67.0% was explained by ASO impairing family relationships (indirect path $\beta_{\text{ASO-BL -> Friendship Support -> AEB-FU}} = 0.03$, standardized estimate = 0.04, z = 4.29, $p < 0.001$; indirect path $\beta_{\text{ASO-BL -> Family Support -> AEB-FU}} = 0.03$, standardized estimate = 0.03, z = 3.81, $p < 0.001$; total path $\beta_{\text{ASO-BL -> AEB-FU}} = 0.04$, standardized estimate = 0.05, z = 2.00, p = 0.046)

Figure 8.2: Mediation of effects of asociality by impacts on relationships with friends and family



Variable	AEB-BL	AEB-FU	ASO-BL	ASO-FU	Friendship Quality	Family Relationship Quality
Covariates	IMD**, Cannabis-BL**, Age**, Ethnic Minority**, Psych. History**, Urbanicity*, Mat.Edu.***	Ethnic Minority*, Mat.Edu.**, Cannabis-BL***	Male**, IMD*, Ethnic Minority**, Psych. History**, Mat.Edu.***	Cannabis-BL*,	Male**, Cannabus-BL***, Age**, Ethnic Minority*	Cannabis-BL**, Mat.Edu.**



Variable	PI-BL	PI-FU	ASO-BL	ASO-FU	Friendship Quality	Family Relationship Quality
Covariates	Male*, IMD*, Age***, Psych. History***, Mat.Edu.**	IMD*, Mat.Edu.*	Mat.Edu.***	-	Male**, Cannabus-BL***, Age**, Ethnic Minority**, Urbanicity*	Cannabis-BL**, Mat.Edu.**

Figure 8.2: Structural equation model diagrams showing mediation effects and significant covariates. Numbers outside of brackets are unstandardized coefficients; standardized coefficients are in brackets. *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$

Of the total ASO -> PI effect, 62.0% was explained by ASO impairing friendships and 40.3% was explained by ASO impairing family relationships (indirect path $\beta_{\text{ASO-BL->Friendship Support-> PI-FU}}$

$= 0.06$, standardized estimate $= 0.05$, $z = 5.52$, $p < 0.001$; indirect path $\beta_{\text{ASO-BL->Family Support->PI-FU}} = 0.04$, standardized estimate $= 0.03$, $z = 4.24$, $p < 0.001$; total path $\beta_{\text{ASO-BL -> PI-FU}} = 0.10$, standardized estimate $= 0.09$, $z = 2.67$, $p = 0.01$).

Direct autoregressive paths remained significant in all mediation models, indicating that detriment to friendships and family relationships does not fully mediate the stability of PE dimensions.

8.4.5 Prediction of depressive symptoms and psychiatric help-seeking

ASO, AEB and PI at baseline showed residual covariance with depressive symptoms (Figure 8.3a). ASO and PI, but not AEB, predicted follow-up depressive symptoms, taking baseline symptoms into account. There was no evidence of either ASO or PI being more predictive of depressive symptoms, shown by a non-significant Satorra-Bentler chi-squared test in which the paths from ASO and PI to follow-up depressive symptoms were constrained to be equal ($\beta_{\text{ASO-BL -> Depressive Symptoms-FU}} = \beta_{\text{PI-BL -> Depressive Symptoms-FU}}$: $\Delta\chi^2 = 0.15$, $\Delta\text{DF} = 1$, $p = 0.70$). See Appendix B for model parameter estimates.

ASO, PI and AEB were higher in those reporting current psychiatric help-seeking at baseline (Figure 8.3b). ASO alone, in addition to baseline psychiatric help-seeking, was predictive of being help-seeking at follow-up.

Figure 8.3: Prediction of future psychopathology by PEs and asociality

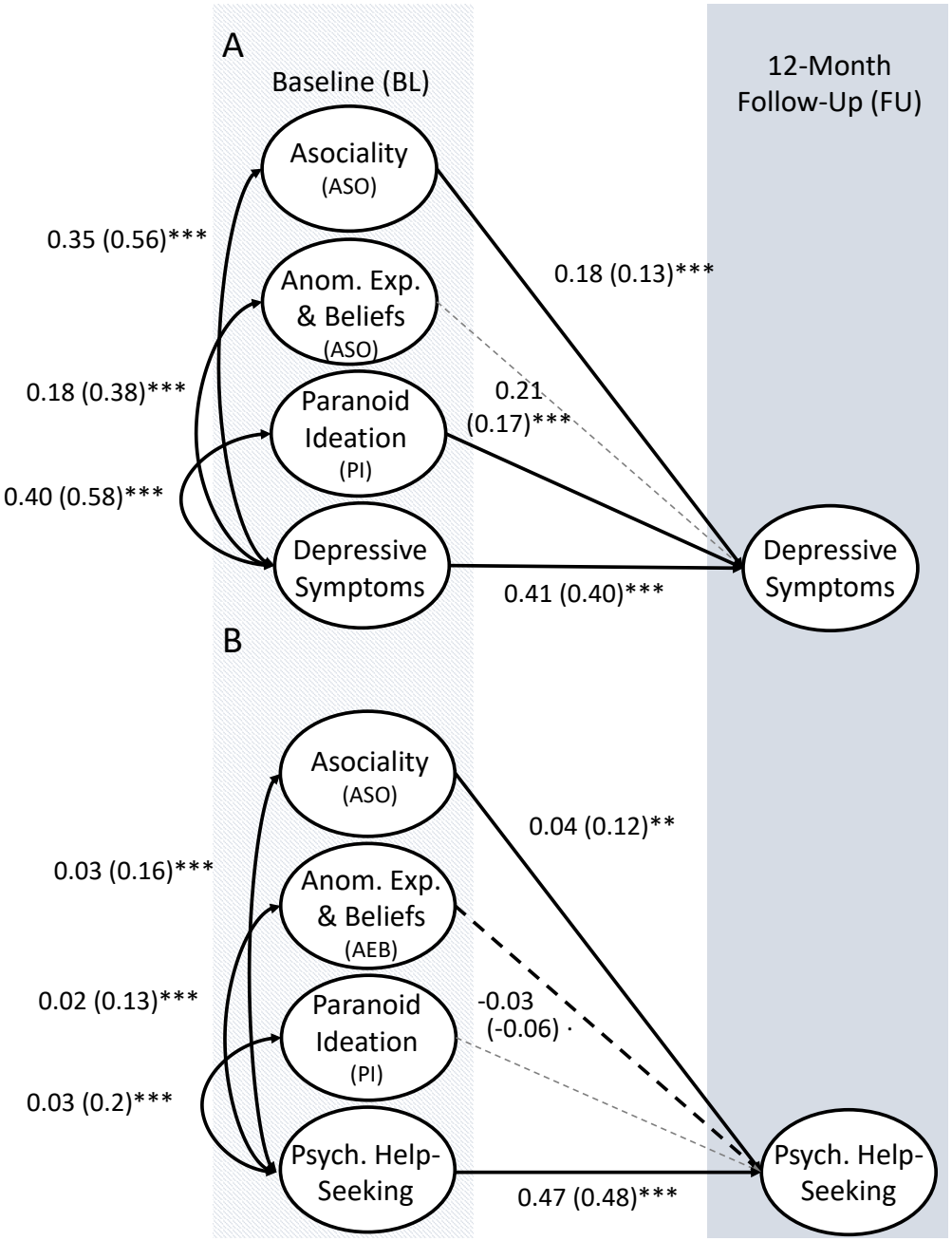


Figure 8.3: Structural equation model diagrams showing prediction of psychopathology by the aspects of the psychosis phenotype. Numbers outside of brackets are unstandardized coefficients; standardized coefficients are in brackets. *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$

8.5 Discussion

Using cross-lagged structural equation modelling in a large, community sample of adolescents and young adults, I showed that anomalous experiences and beliefs (AEB), paranoid ideation (PI) and asociality (ASO), while being relatively stable, interact during development. ASO in young people predicts greater positive psychotic phenomena (AEB and PI) twelve months later, but

neither AEB nor PI predict future ASO. These effects are fully mediated by detrimental effects of ASO on quality of friendships and family relationships. ASO and PI are both associated with future depressive symptoms, while ASO is associated with future psychiatric help-seeking. AEB, controlling for ASO and PI, was not associated with future depressive symptoms or help-seeking. These results support a temporal precedence in which asociality precedes emergence or increase of positive psychotic phenomena. Building on the results of clustering analyses in Chapter 7, these results support that asocial dispositions, poor quality of social relationships and paranoid thoughts and beliefs are detrimental to mental health and are so to a greater extent than non-paranoid unusual perceptions and beliefs.

The study was strengthened by use of a large, epidemiologically-principled cohort sample of adolescents and young adults. Inference was greatly strengthened by ensuring the same latent variables were measured over time (measurement invariance), an improvement on previous work on this question (Collip et al., 2013). While the effect of poorer social functioning predicting psychotic phenomena has previously been shown, it has not been subjected to mediation analyses to show that this effect is explained by impairments to both friendships and family relationships. I also controlled for a number of relevant confounders including psychiatric help-seeking and drug use.

This study also has limitations. The Schizotypal Personality Questionnaire, measures additional dimensions that I did not use in this study, including odd perceptions of one's self and social anxiety, that may be important aspects of a broader psychosis phenotype. With data from only two waves of data collection, I was not able to establish temporal precedence in mediation and so our results should be replicated in a sample with better temporal resolution. Cross-lagged modelling estimates a single population trajectory so it will be necessary to examine different trajectories in sub-populations.

Chapter 9

Different longitudinal relationships between childhood adversity, adolescent/adult social support and dimensions of depressive and psychotic symptoms in two general population cohorts

Abstract

Childhood adversity and poor social support are implicated in the development of psychosis but have rarely been investigated together. This study investigated longitudinal relationships in adolescents and young adults between childhood adversity, adolescent/adult social support and later dimensions of depressive symptoms (DS) and psychotic experiences, measured as paranoid ideation (PI) and non-paranoid anomalous experiences & beliefs (AEB). Data came from two longitudinal general population cohorts (ROOTS: N = 1238, assessed at age 14 (baseline) & 17; NSPN: N = 1919, age 16-25, assessed at baseline and one-year follow-up). Self-report DS, AEB and PI were measured at age 17 in ROOTS and at follow-up in NSPN. Childhood adversity was measured retrospectively at baseline with a structured interview with caregivers in ROOTS and a self-report questionnaire in NSPN. Self-report social support from friends and family were measured at baseline in both cohorts. Longitudinal relationships were tested by estimating structural equation models with robust full-information maximum likelihood. The models had direct paths from childhood adversity to DS, PI & AEB, from childhood adversity to social support and from social support to symptom outcomes. Sex, non-white ethnicity, age (NSPN), socioeconomic deprivation, cannabis use, family history of mental disorder and maternal years of education were included as covariates. Childhood adversity had direct effects promoting all symptom outcomes, even when considering its effects on later social support and the effects of support on symptoms. Childhood adversity impaired later support from family in ROOTS and support from family and friends in NSPN. Social support from family and friends reduced depressive symptoms and paranoid ideation in both cohorts. AEB was less affected by social support; social support from friends reduced AEB in NSPN but with a smaller effect size than for DS and PI.

No other social support variables affected AEB. Parts of the effects of childhood adversity on symptoms were mediated by poorer family support in ROOTS (mediated by family support: DS = 16.5%, PI = 14.2%) and by poorer family and friendship support in NSPN (mediated by family support: DS = 29.5%, PI = 14.7%; mediated by friendship support: DS = 15.4%, PI = 20%, AEB = 10.8%). Childhood adversity may have long-lasting effects predisposing to some unusual experiences & beliefs that may not be greatly modifiable by positive social relationships in later life, while paranoid ideation and depressive symptoms may be more affected by recent social support. Some of the detrimental effects of childhood adversity on mental health may be attributed to poorer quality of relationships later in life. Good social support might not eliminate all psychotic experiences but may lower paranoia and distress, mitigating some effects of early-life adversity.

9.1 Research Questions

- How are childhood adversity and recent social support related to one another and to later manifestation of distress and PEs?

9.2 Introduction

Childhood adversity is a risk factor for psychotic experiences (PEs) and psychotic disorders (Varese et al., 2012). Childhood adversity is potentially associated with both potentially 'benign' PEs in people with no need for clinical care (Brett et al., 2007; Daalman et al., 2012) as well as 'maladaptive' PEs that occur in psychotic disorders.

Childhood adversity may cause PEs via a number of proposed mechanisms, including post-traumatic dissociation (Morrison, 2001; Kilcommons and Morrison, 2005), attachment difficulties (Berry et al., 2007), induction of negative schema and cognitive biases (Garety and Kuipers, 2001; Smith et al., 2006) and increased sensitivity to stress (Zubin and Spring, 1977; Nuechterlein and Dawson, 1984).

Poor social support in later life is also implicated in the aetiology and course of PEs and psychotic disorder (Gayer-Anderson and Morgan, 2013). Social support comprises social networks, 'enacted' support that is actually provided in times of stress and 'perceived' support of how supported a person feels by social relationships. Psychotic illness is associated with poor social support, both in chronic (Beels, 1981; Buchanan, 1995; Meesters et al., 2010) and early disease stages (Gayer-Anderson and Morgan, 2013). Poor premorbid levels of functioning and social integration predict later psychosis (Malmberg et al., 1998; Cannon et al., 2008; Velthorst et al., 2009; Dragt et al., 2011), with progressive impairment leading up to onset of psychotic disorder (Velthorst et al., 2016).

Social support is thought to be a critical component of resilience to stress (Cohen and Wills, 1985) and could interact with the proposed psychosis-promoting mechanisms of adversity. Supportive relationships through friends, family or other social environments may promote the normalisation and adaptive appraisal of aberrant experiences (Claridge, 1997; Farias et al., 2013; Peters et al., 2016), tend away from negative schema (Brown et al., 1986) and negative affect (Powers et al., 2009), reduce the stress that aberrant experiences cause (Brett et al., 2014) and act

as a general buffer against stress from all causes. However, relatively little is known about the relationships between PEs/psychotic disorders, adversity in childhood and social support in later life. In Chapter 5, I reported that a non-distressed, PE-prone phenotype (NDPE), identified using two clustering methods in both NSPN and ROOTS, two cohorts of adolescents and young adults, was similarly associated with childhood adversity when compared to a distressed, PE-prone phenotype (DPE), who were at greater psychiatric risk. The groups also showed different profiles of PEs, with NDPE and DPE having similar levels of self-report non-paranoid anomalous experiences and beliefs (AEB) and interview-verified hallucinations and anomalous experiences, but the NDPE had lower self-report paranoid ideation (PI) and interview-verified delusions. On investigating features of their social environment, these phenotypes had similar exposure to childhood adversity, but strikingly different perceived social support from family and friends, with far better support in the NDPE phenotype in all samples. In ROOTS, this pattern of differences in support was present at age 14, 3 years prior to the time of clustering at age 17.

The different profiles of PE dimensions and distress across the NDPE and DPE phenotypes, may indicate that childhood adversity and later social support have different associations with symptom outcomes in adolescents and young adults. Specifically, high AEB co-occurred with childhood adversity but with both good and poor support, while high PI and high depressive symptoms were associated with both adversity and poor support. We might hypothesise that social support particularly minimises paranoia and distress but does not necessarily affect other non-paranoid unusual perceptions or beliefs. Childhood adversity could predispose to all dimensions or principally to AEB.

To understand these associations, we need to disentangle the pathways between childhood adversities and later social support. Unfortunately, family-focused adversities, including severe adversities like physical abuse and sexual abuse, tend to cluster together and be stable over childhood and adolescence (Dunn et al., 2011). Family-focused adversity in childhood predicts poorer quality of family relationships later in life, and peer-focused adversity, like bullying, predicts poorer quality of friendships (van Harmelen et al., 2016). Progress on this question is limited by reliance usually on retrospective and cross-sectional measurements and the fact that social support and childhood adversity have rarely been considered together (Gayer-Anderson et al., 2015). Associations between childhood adversity and PEs might be partly or wholly driven by early adversity impairing later social support, which promotes PEs. Alternatively, childhood adversity and later social support may be independent risk/protective factors for PEs, with the effects of adversity being mitigated by good social support and exacerbated by poor support.

In this chapter, I designed analyses to investigate whether outcomes of AEB, PI and DS were differently affected by childhood adversity and later social support and whether any of the established association between childhood adversity and PEs may be driven by impairments of support in later life. To do this, I used structural equation modelling (SEM), an extension of latent variable modelling, in NSPN and ROOTS. The SEM framework allowed me to estimate all relationships between these variables simultaneously while controlling for a number of potentially relevant covariates and appropriately accounting for missing data. I planned first to confirm that I could adequately measure symptom outcomes (AEB, PI and DS) by simultaneously estimating latent variables for each. I extended this model to firstly investigate how symptom

outcomes were affected by childhood adversity and then secondly investigate how these associations changed when recent social support as incorporated. Using model comparison, I planned to test whether associations in these pathways were non-zero and differed from one another. Using mediation analyses, I planned to test whether the effects of childhood adversity on symptom outcomes could partly or fully be explained by impairing support later in life.

9.3 Methods

9.3.1 Data

Data come from ROOTS and NSPN. For full information, see Methodology. In NSPN, the questionnaire measuring childhood adversity (see below) measured adversity between ages of 0-16, while some participants were aged 14-15. For these analyses, I therefore used only participants aged 16 or older from NSPN.

9.3.2 Instruments

Psychotic phenomena (Anomalous Experiences & Beliefs, Paranoid Ideation)

In ROOTS, positive psychotic phenomena were measured using two subscales from the Brief Schizotypal Symptoms Inventory (BSSI), a 20-item self-report instrument measuring psychotic phenomena in the last two weeks. The AEB subscale comprises perceptual abnormalities and magical thinking (8 items). The PI subscale comprises suspiciousness and ideas of reference (6 items, of which one is redundant). I showed in chapter 3 that the AEB and PI scales measure the same underlying psychosis factor as a semi-structured interview method (Horwood et al., 2008) with high measurement precision over a broad range of PE intensity.

Questions were structured as a set of statements or questions. Participants indicated how often that statement applied to them in the last two weeks on a 5-point scale ('Not at all', 'Occasionally', 'Sometimes', 'Often' and 'All the time'. Due to low endorsement of some categories, responses were collapsed into a 3-point scale ('Not at all', 'Occasionally', 'Sometimes/Often/All the time'). SSI scales are likely to be unidimensional (ω_{H}: = AEB = 0.71, PI = 0.88) and have high internal consistency (ω_{T}: AEB = 0.93, PI = 0.93) (Revelle and Zinbarg, 2009). For further information, see chapter 2.

In NSPN, self-report psychotic phenomena were measured with the Schizotypal Personality Questionnaire (SPQ), which comprises 74 dichotomous items intended to measure general, trait-like experience of 9 dimensions associated with psychosis-proneness. In Chapter 2, I showed that, while these 9 dimensions are reliable, a number are likely to be redundant. While second-order latent variable models suggest three or four variables explain scores on these subscales, they are not reliable when estimated at the item level. Instead, I identified a reliable 6-factor solution without redundantly high correlations among factors. Of relevance for this study are the dimensions most similar to typical psychotic phenomena: 'Anomalous Experiences & Beliefs' ($\mathrm{AEB}_{\mathrm{SPQ}}$), comprising 18 items measuring unusual perceptual experiences and magical think-

ing and 'Paranoid Ideation' (PI_{SPQ}), comprising 13 items measuring suspiciousness and ideas of reference. For further information, see chapter 2.

Depressive symptoms

In both cohorts, self-report DS were measured with the Mood and Feelings Questionnaire (MFQ) (Costello and Angold, 1988). The full questionnaire comprises 33 items on common symptoms of depression and anxiety occurring over the last two weeks. The full MFQ is likely to be multidimensional (Brodbeck et al., 2011) and has a fairly large number of items, which is computationally demanding when fitting latent variable models. I therefore used the items that comprise the Short Mood and Feelings Questionnaire (SMFQ), which are contained within the full MFQ. These items were used previously in identifying a common factor underlying mood, anxiety and psychotic experiences. The SMFQ is likely to be unidimensional and is able to predict clinical depression and anxiety with reasonable sensitivity (Messer et al., 1995; Turner et al., 2014).

Family-focused childhood adversity

I compared phenotypes in ROOTS on childhood adversity, measured using the Cambridge Early-Experiences Interview (Dunn et al., 2011), a semi-structured caregiver interview measured at the first time point (proband age 14). I used a sum score of any family loss, moderate/severe family discord, abuse (physical/sexual/emotional), family criminality, financial problems and unemployment, maternal psychiatric illness, paternal psychiatric illness, aberrant parenting styles (either parent) and lack of maternal affection/engagement.

In NSPN, adversity between ages 0-16 was measured using the self-report Measures of Parenting Style (MOPS) questionnaire (Parker et al., 1997), with subscales of abuse, indifference and overbearingness measured for mothers and fathers independently. I used a sum score of all subscales for both parents.

Social support

Perceived social support from friends was measuring using the Friendship Quality scale of the Cambridge Friendships Questionnaire (van Harmelen et al., 2016). Perceived social support from family members was measured using the General Functioning scale of the McMasters Family Assessment Device (Epstein and Baldwin, 1983).

Covariates

Covariates included were: sex, non-white ethnicity, age (in NSPN), socioeconomic deprivation (estimated from post-codes; ROOTS: ACORN category of 'hard-pressed', http://www.caci.co.uk; NSPN: socioeconomic deprivation (overall country ranking), https://www.gov.uk/government/collections/englis indices-of-deprivation), family history of psychiatric illness, cannabis use and maternal years of education (ROOTS) or maternal qualifications (NSPN).

9.3.3 Viability of sum scores and internal consistency

I assessed the psychometric properties of the instruments measuring CA, family support (FAD-GF) and friendship support (CFQ-FQ) using bifactor modelling of each scale (see Empirical Chapter 1 for methods). Sum scores were used if a bifactor model (with a general factor and three specific factors) could be fit to the observed data and the proportion of variance explained by the general factor ('general factor saturation', (ω_H) exceeded 0.5 (Revelle and Zinbarg, 2009). I report the variance explained by the general factor and all specific factors (ω_T) as an indicator of internal consistency (Revelle and Zinbarg, 2009). I estimated bifactor models from polychoric correlations to account for ordinal data on the CAMEEI, FAD-GF and CFQ-FQ and Pearson correlations for the subscale scores on the MOPS.

9.3.4 Structural equation models

To ensure that the models adequately explained observed data on symptom outcomes, 'measurement' models of the three latent outcome variables (AEB, PI and SMFQ) were first estimated, with covariates included by adding regression paths to each latent outcome variable. To test the effects of the social environment, measurement models were then extended to 'structural' models (Figure 9.1). Childhood adversity and social support were included by regression paths from them to latent symptom outcomes. Covariates were included by adding regression paths to latent symptom outcomes and to adversity and support variables, where present. 'Adversity' structural models tested the effects of childhood adversity alone with regression paths from CA to the outcome variables. 'Adversity & support' structural models simultaneously tested effects of adversity, support and their inter-relationships. These models included regression paths from CA to symptom outcome variables, testing the 'direct paths' from CA to symptoms. These models also included regression paths from CA to social support variables, then from social support variables to the outcomes. The latter paths tested the effects of social support on outcomes and, when combined with the former, make up the multi-step 'indirect paths' from CA to symptoms via effects on social support.

Regression coefficients and standard errors for indirect paths and 'total paths' (combined direct and indirect) were quantitatively estimated using the delta method. I estimated the size of mediation effects by comparing the standardized coefficients of indirect paths with the standardized coefficient of the total paths (Iacobucci, 2012).

Variables like CA and social support and ordinally-measured item responses were expected to be non-normally distributed. All models were therefore fit with a robust maximum-likelihood (MLR) estimator with robust (Huber-White) standard errors and Satorra-Bentler scaled test statistics. Fit was assessed using CFI & TLI (both > 0.9), the RMSEA (< 0.08) and the SRMR (< 0.06). I calculated the RMSEA of the null model (with no associations between variables), because when the null model fits well (RMSEA < 0.158), fit indices based on comparison between the actual model and null model (CFI & TLI) will be too low and less useful (Kenny, n.d.). Missing data were estimated using full-information maximum likelihood.

Nonsignificant paths were retained in order to minimise empirical re-specification of models. I reported unstandardized and standardized path coefficients, their standard errors and their sig-

Figure 9.1: Structural equation model structures tested

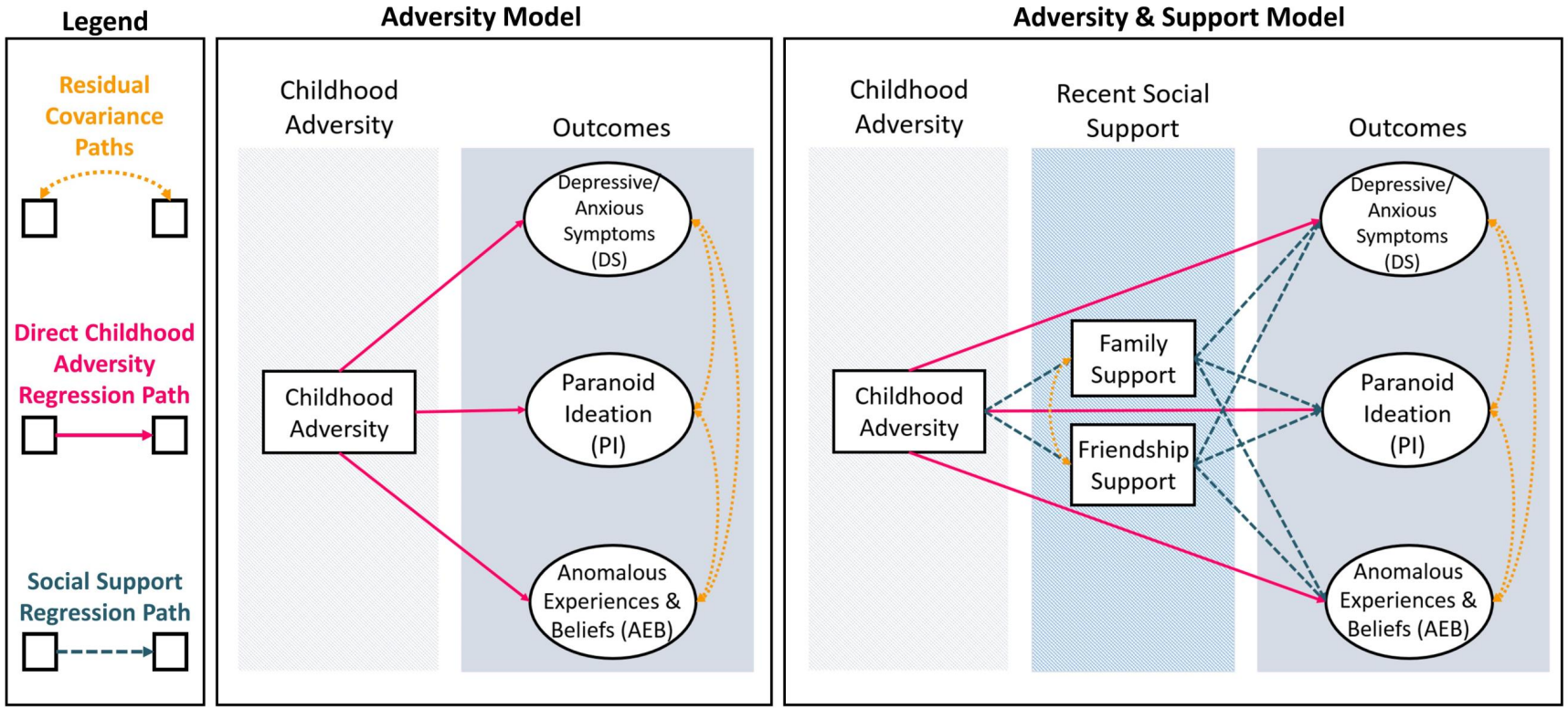


Figure 9.1: General structure of models tested using data from the ROOTS and NSPN cohorts.

nificance based on Wald tests. Significance and difference between regression paths of interest were additionally tested using the Satorra-Bentler Chi-Squared test, in which a model was estimated with the regression coefficient (β) of the path of interest constrained to 0 or equal to another path coefficient and fit compared to a model in which the path coefficient was freely estimated. A significant result, meaning that constraining that path coefficient resulted in poorer model fit, confirmed that a path is non-zero or is different to another path.

SEMs were fit using the *lavaan* (Rosseel, 2012) package in R, supplemented by functions from *semTools* (semTools Contributors, 2016).

9.4 Results

9.4.1 Data

Table 9.1: Descriptive statistics.

Instrument	Variable	N Complete Data	Mean	Standard error	Median	Median Absolute Deviation	Range
Self-Report	Male	2388	0.47	0.5	0	0	1
Self-Report	Socioeconomic deprivation (IMD)	2376	-0.01	1	0.17	1.24	3.31
Self-Report	Cannabis use at baseline	2388	0.12	0.33	0	0	1
Self-Report	Age (years)	2388	19.08	3.01	18.7	3.51	11.06
Self-Report	Non-white ethnicity	2388	0.23	0.42	0	0	1
Self-Report	Any family psychiatric history	2388	0.11	0.31	0	0	1
Self-Report	Urban-Rural Indicator	2376	5.47	0.75	5	0	5
Self-Report	Maternal educational qualifications	2388	1.73	1.11	2	1.48	3
FAD (Follow-up)	Family support	1646	0	1	0	1.16	3.76
CFQ (Follow-up)	Friendship support	1667	0	1	0.09	1.01	4.08

Table 9.1 – continued from previous page

Instrument	Variable	N Complete Data	Mean	Standard error	Median	Median Absolute Deviation	Range
Self-Report	Current psychiatric help-seeking (Baseline)	2370	0.06	0.23	0	0	1
Self-Report	Current psychiatric help-seeking (Follow-up)	1634	0.06	0.23	0	0	1
SMFQ (Baseline)	Depressive symptoms	2322	7.36	5.49	6	4.45	26
SMFQ (Follow-up)	Depressive symptoms	1770	6.77	5.53	5	4.45	26

Table 9.1: Descriptive statistics of covariates, social support from friends and family and psychopathology variables.

In ROOTS, 1238 participants took part at time 1 (age 14) and 1074 took part at time 3 (age 17, 86.8% retention). In NSPN, 2388 participants returned questionnaire packs at time 1, with 1919 between the ages of 16-25 included in this study. 1808 of the 2388 returned questionnaire packs one year later at time 2 (75.7% retention). Measures of CA (CAMEEI in ROOTS, MOPS in NSPN), family support (FAD-GF) and friendship support (CFQ-FQ) showed adequate unidimensionality (ω_H) and good internal consistency (ω_T) in ROOTS (CA: ($\omega_H = 0.77$, ($\omega_T = 0.92$; family support: ($\omega_H = 0.79$; ($\omega_T = 0.94$; friendship support: ($\omega_H = 0.68$; ($\omega_T = 0.92$) and in NSPN (CA: ($\omega_H = 0.57$; ($\omega_T = 0.89$; family support: ($\omega_H = 0.84$; ($\omega_T = 0.96$; friendship support: ($\omega_H = 0.73$; ($\omega_T = 0.91$)

2388 participants returned questionnaire packs at time 1 (aged 14-25) and 1808 returned questionnaire packs one year later at time 2 (75.7% retention). At baseline, 2106 participants had complete data on all 74 SPQ items and 2352 had missing data on 5 or fewer items. At follow-up, 1546 had complete data on all SPQ items and 1668 had missing data on 5 or fewer items. Descriptive statistics, including number of complete/missing responses on covariates and social support/psychopathology variables used in latent variable modelling, are shown in Table 9.1.

Multivariate logistic regressions showed that missingness on each variable was predicted by one or more of sex, non-white ethnicity, socioeconomic deprivation, level of maternal education, cannabis use or age (in NSPN), supporting that data meet missing-at-random (MAR) assumptions required for fiML estimation. All continuous observed variables were mean-centred and scaled to unit variance.

9.4.2 Fit of measurement models for symptom outcomes

The measurement model of AEB, PI and DS fit well in both ROOTS (χ^2 = 1380.035, DF = 434, p < 0.001, RMSEA (95% CI) = 0.042 (0.040 – 0.044), SRMR = 0.050, $RMSEA_{NULL}$ = 0.126, CFI* = 0.872, TLI* = 0.858) and in NSPN (χ^2 = 4532.695, DF = 1186, p < 0.001, RMSEA (95% CI) = 0.034 (0.033 – 0.035), SRMR = 0.048, $RMSEA_{NULL}$ = 0.094, CFI* = 0.838, TLI* = 0.828; * = null RMSEA too low for CFI/TLI to be meaningful).

9.4.3 Childhood adversity is associated with depressive symptoms, anomalous experiences & beliefs and paranoid ideation

Table 9.2: Results of Wald tests of regression parameters being equal or zero in longitudinal structural equation models of childhood adversity predicting later depressive symptoms and psychotic phenomena.

Model	β	χ^2	ΔDF	P-value
ROOTS	$\beta_{\text{CA -> DS}} = 0$	19.7	1	<0.001
	$\beta_{\text{CA -> AEB}} = 0$	6.56	1	0.01
	$\beta_{\text{CA -> PI}} = 0$	7.16	1	0.007
	$\beta_{\text{CA -> DS}} = \beta_{\text{CA -> AEB}} = \beta_{\text{CA -> PI}}$	0.08	2	0.96
	$\beta_{\text{CA -> DS}} = \beta_{\text{CA -> AEB}}$	0.07	1	0.795
	$\beta_{\text{CA -> DS}} = \beta_{\text{CA -> PI}}$	<0.001	1	0.962
	$\beta_{\text{CA -> PI}} = \beta_{\text{CA -> AEB}}$	0.06	1	0.802
NSPN	$\beta_{\text{CA -> DS}} = 0$	124.2	1	<0.001
	$\beta_{\text{CA -> AEB}} = 0$	72.66	1	<0.001
	$\beta_{\text{CA -> PI}} = 0$	116.74	1	<0.001
	$\beta_{\text{CA -> DS}} = \beta_{\text{CA -> AEB}} = \beta_{\text{CA -> PI}}$	41.44	2	<0.001
	$\beta_{\text{CA -> DS}} = \beta_{\text{CA -> AEB}}$	30.85	1	<0.001
	$\beta_{\text{CA -> DS}} = \beta_{\text{CA -> PI}}$	0.49	1	0.483
	$\beta_{\text{CA -> PI}} = \beta_{\text{CA -> AEB}}$	31.31	1	<0.001

Table 9.2: CA = Childhood adversity. DS = depressive symptoms. AEB = Anomalous Experiences & Beliefs. PI = Paranoid Ideation.

The adversity structural model fit well in ROOTS and NSPN (see Figure 9.2). For full model parameter estimates, see Appendix B. For results of path testing, see Table 9.2. CA was associated with DS, AEB and PI in both cohorts. In ROOTS, these associations did not differ. In NSPN, the associations between CA and DS and PI were equal and greater than the association between CA and AEB.

Figure 9.2: Relationships between childhood adversity, PEs and depressive symptoms

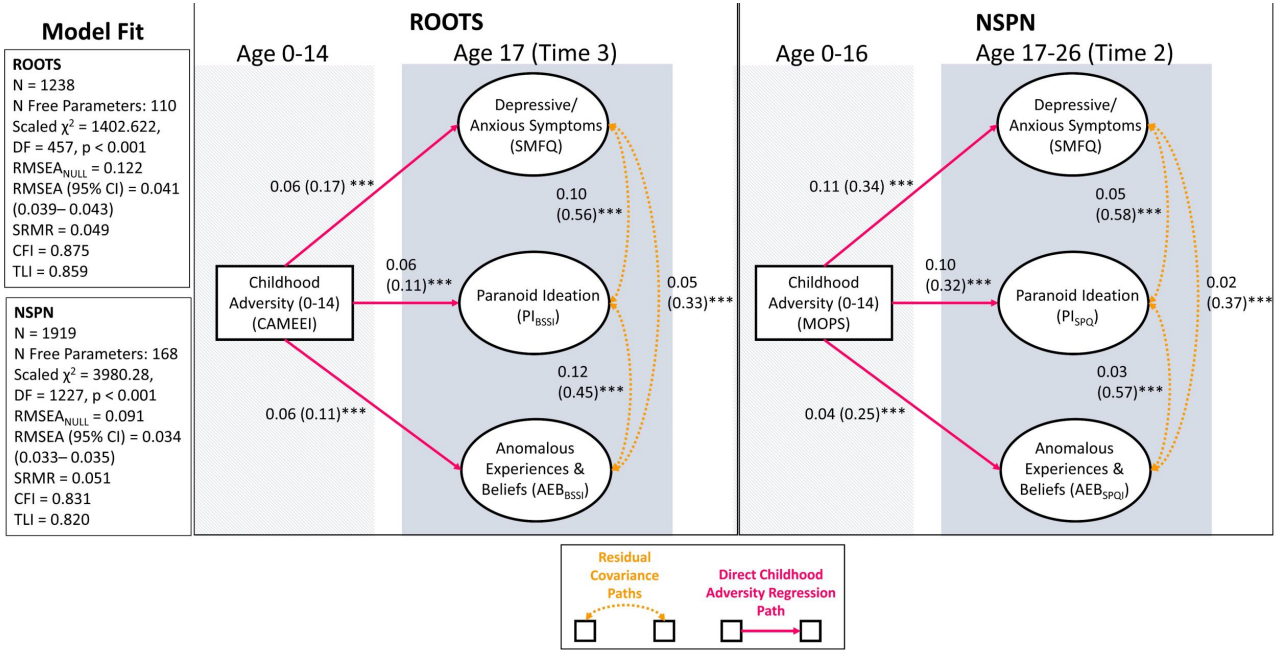


Figure 9.2: Direct adversity models in NSPN and ROOTS. Fit indices are shown on the left (Cut-off values: RMSEA < 0.08, SRMR < 0.06, CFI & TLI > 0.9 (if RMSEA of null model < 0.156). Numbers on paths indicate unstandardized path coefficients, with standardized coefficients in brackets. *** = $p < 0.001$, ** = $p < 0.01$, * = $p < 0.05$

9.4.4 Childhood adversity has direct effects with social support considered. Social support lowers depressive symptoms and paranoid ideation more than anomalous experiences & beliefs

Table 9.3: Results of Wald tests of regression parameters being equal or zero in longitudinal structural equation models relationships between childhood adversity, social support, depressive symptoms and psychotic phenomena.

Cohort	β	χ^2	ΔDF	P-value
ROOTS	$\beta_{\text{CA -> DS}} = 0$	13.86	1	<0.001
	$\beta_{\text{CA -> AEB}} = 0$	5.24	1	0.022
	$\beta_{\text{CA -> PI}} = 0$	4.3	1	0.038
	$\beta_{\text{CA -> DS}} = \beta_{\text{CA -> AEB}} = \beta_{\text{CA -> PI}}$	0.06	2	0.971
	$\beta_{\text{CA -> DS}} = \beta_{\text{CA -> AEB}}$	0.05	1	0.817
	$\beta_{\text{CA -> DS}} = \beta_{\text{CA -> PI}}$	0.02	1	0.881
	$\beta_{\text{CA -> PI}} = \beta_{\text{CA -> AEB}}$	0.05	1	0.82
	$\beta_{\text{CA -> Family}} = 0$	18.15	1	<0.001
	$\beta_{\text{CA -> Friendship}} = 0$	1.52	1	0.218
	$\beta_{\text{CA -> Family}} = \beta_{\text{CA -> Friendship}}$	4.27	1	0.039
	$\beta_{\text{Family -> DS}} = 0$	25.24	1	<0.001
	$\beta_{\text{Family -> AEB}} = 0$	3.38	1	0.066
	$\beta_{\text{Family -> PI}} = 0$	17.61	1	<0.001
	$\beta_{\text{Family -> DS}} = \beta_{\text{Family -> AEB}} = \beta_{\text{Family -> PI}}$	5.92	2	0.052
	$\beta_{\text{Family -> DS}} = \beta_{\text{Family -> AEB}}$	5.63	1	0.018
	$\beta_{\text{Family -> DS}} = \beta_{\text{Family -> PI}}$	2.28	1	0.131
	$\beta_{\text{Family -> PI}} = \beta_{\text{Family -> AEB}}$	2.09	1	0.148
	$\beta_{\text{Friendships -> DS}} = 0$	10.28	1	0.001
	$\beta_{\text{Friendships -> AEB}} = 0$	0.06	1	0.801
	$\beta_{\text{Friendships -> PI}} = 0$	9.36	1	0.002
	$\beta_{\text{Friendships -> DS}} = \beta_{\text{Friendships -> AEB}} = \beta_{\text{Friendships -> PI}}$	6.95	2	0.031
	$\beta_{\text{Friendships -> DS}} = \beta_{\text{Friendships -> AEB}}$	8.04	1	0.005
	$\beta_{\text{Friendships -> DS}} = \beta_{\text{Friendships -> PI}}$	1.73	1	0.188
	$\beta_{\text{Friendships -> PI}} = \beta_{\text{Friendships -> AEB}}$	10.5	1	0.001
NSPN	$\beta_{\text{CA -> DS}} = 0$	27.64	1	<0.001
	$\beta_{\text{CA -> AEB}} = 0$	29.94	1	<0.001
	$\beta_{\text{CA -> PI}} = 0$	35.41	1	<0.001

Table 9.3 – continued from previous page

Cohort	β	χ^2	ΔDF	P-value
	$\beta_{\text{CA -> DS}} = \beta_{\text{CA -> AEB}} = \beta_{\text{CA -> PI}}$	6.17	2	0.046
	$\beta_{\text{CA -> DS}} = \beta_{\text{CA -> AEB}}$	5.71	1	0.017
	$\beta_{\text{CA -> DS}} = \beta_{\text{CA -> PI}}$	0.14	1	0.703
	$\beta_{\text{CA -> PI}} = \beta_{\text{CA -> AEB}}$	2.84	1	0.092
	$\beta_{\text{CA -> Family}} = 0$	486.02	1	<0.001
	$\beta_{\text{CA -> Friendship}} = 0$	133.6	1	<0.001
	$\beta_{\text{CA -> Family}} = \beta_{\text{CA -> Friendship}}$	61.9	1	<0.001
	$\beta_{\text{Family -> DS}} = 0$	40.15	1	<0.001
	$\beta_{\text{Family -> AEB}} = 0$	<0.001	1	0.952
	$\beta_{\text{Family -> PI}} = 0$	8.35	1	0.004
	$\beta_{\text{Family -> DS}} = \beta_{\text{Family -> AEB}} = \beta_{\text{Family -> PI}}$	38.65	2	<0.001
	$\beta_{\text{Family -> DS}} = \beta_{\text{Family -> AEB}}$	10.25	1	0.001
	$\beta_{\text{Family -> DS}} = \beta_{\text{Family -> PI}}$	9.37	1	0.002
	$\beta_{\text{Family -> PI}} = \beta_{\text{Family -> AEB}}$	41.08	1	<0.001
	$\beta_{\text{Friendships -> DS}} = 0$	34.81	1	<0.001
	$\beta_{\text{Friendships -> AEB}} = 0$	15.35	1	<0.001
	$\beta_{\text{Friendships -> PI}} = 0$	55.45	1	<0.001
	$\beta_{\text{Friendships -> DS}} = \beta_{\text{Friendships -> AEB}} = \beta_{\text{Friendships -> PI}}$	30.16	2	<0.001
	$\beta_{\text{Friendships -> DS}} = \beta_{\text{Friendships -> AEB}}$	31.2	1	<0.001
	$\beta_{\text{Friendships -> DS}} = \beta_{\text{Friendships -> PI}}$	2.21	1	0.138
	$\beta_{\text{Friendships -> PI}} = \beta_{\text{Friendships -> AEB}}$	10.39	1	0.001

Table 9.3: CA = Childhood adversity. DS = depressive symptoms. AEB = Anomalous Experiences & Beliefs. PI = Paranoid Ideation.

The adversity & support model fit well in ROOTS (Figure 9.3) and NSPN (Figure 9.4). For full model parameters, see Appendix B. For results of path testing, see Table 9.3.

In ROOTS, with social support at 14 included in the model, CA was still directly associated with DS and AEB, and there was a trend-level association with PI. The size of these direct CA associations did not differ. In NSPN, CA was still directly associated with DS, AEB and PI. These direct CA associations differed overall and the association between CA and DS was stronger than that between CA and AEB.

In ROOTS, social support from family and from friends was associated with lower DS and PI, but not AEB. The sets of associations between both types of social support and DS, AEB and PI differed overall. In both cases, the only pair-wise difference was that social support was more strongly associated with lower DS than lower AEB. There was a trend towards social support

Figure 9.3: Longitudinal relationships between childhood adversity, social support, PEs and depressive symptoms in ROOTS

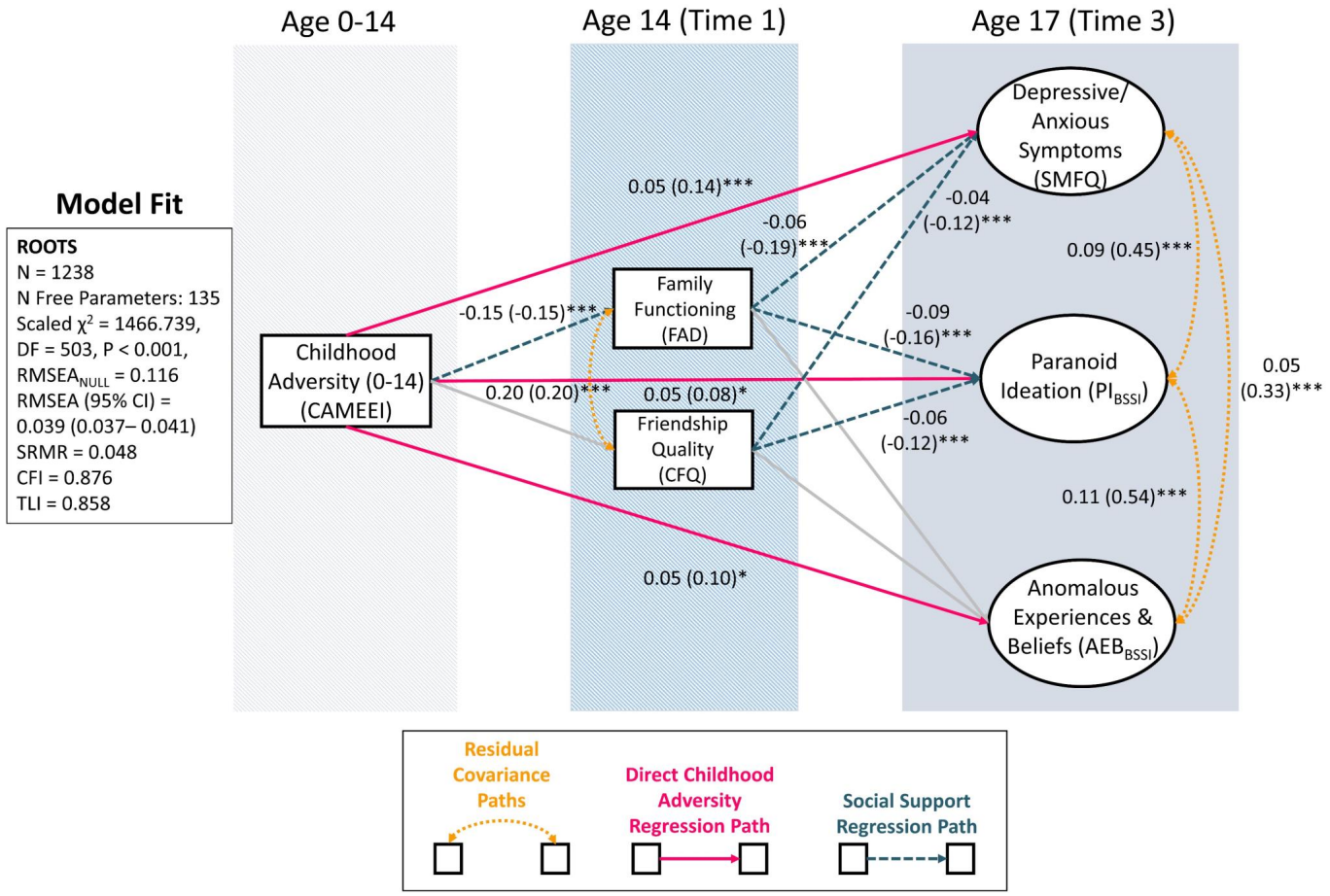


Figure 9.3: Results of adversity and support model in ROOTS. Fit indices are shown on the left (Cut-off values: RMSEA < 0.08, SRMR < 0.06, CFI & TLI > 0.9 (if RMSEA of null model < 0.156). Greyed out paths indicate non-significance ($p > 0.05$). Numbers on paths indicate unstandardized path coefficients, with standardized coefficients in brackets. *** $= p < 0.001$, ** $= p < 0.01$, * $= p < 0.05$.

Figure 9.4: Longitudinal relationships between childhood adversity, social support, PEs and depressive symptoms in NSPN

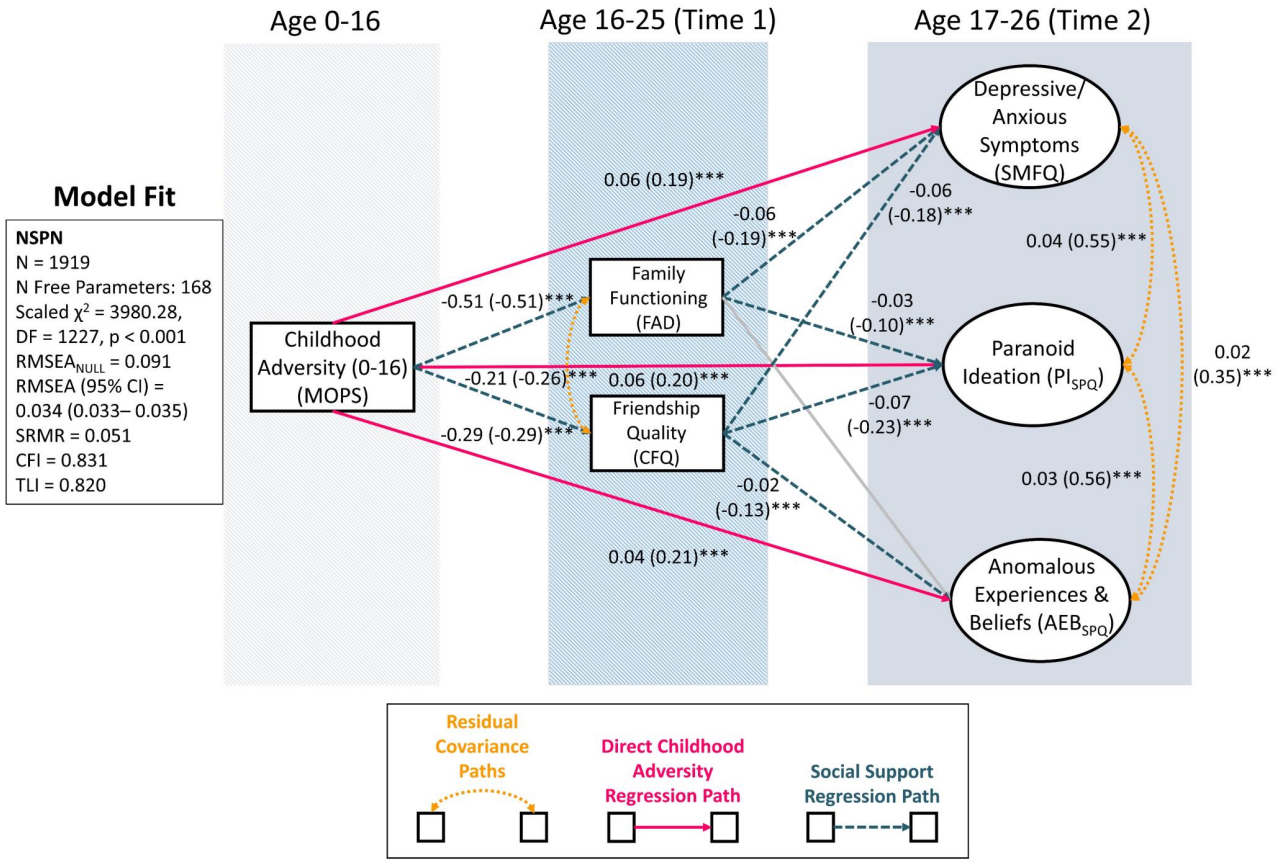


Figure 9.4: Results of adversity and support model in NSPN. Fit indices are shown on the left (Cut-off values: RMSEA < 0.08, SRMR < 0.06, CFI & TLI > 0.9 (if RMSEA of null model < 0.156). Greyed out paths indicate non-significance ($p > 0.05$). Numbers on paths indicate unstandardized path coefficients, with standardized coefficients in brackets. *** = $p < 0.001$, ** = $p < 0.01$, * = $p < 0.05$.

from family being associated with lower PI than lower AEB.

In NSPN, social support from family was associated with lower DS and PI, but not AEB. Family support lowered DS more strongly than PI, and lowered both more than AEB, supported by significant differences between all three paths. Social support from friendships was associated with lower DS, PI and AEB. Friendship support lowered DS and PI equally and lowered both more than it did AEB, supported by an overall difference and pair-wise differences in all associations apart from between friendship support and DS and PI.

9.4.5 Mediation analyses

Table 9.4: Results of Wald tests of regression parameters being equal or zero in longitudinal structural equation models of childhood adversity predicting later depressive symptoms and psychotic phenomena.

Cohort	Path	Unstd. estimate	Std. error	z	P-value	Std. estimate	% mediated
ROOTS	CA -> Family support -> DS	0.01	0	3.26	0.001	0.03	16.5
	CA -> Friendship support -> DS	0	0	1.11	0.269	0.01	-
	Total ->DS	0.06	0.01	4.33	< 0.001	0.17	-
	CA -> Family support -> AEB	0	0	1.63	0.102	0.01	-
	CA -> Friendship support -> AEB	0	0	0.2	0.843	0	-
	Total -> AEB	0.06	0.02	2.63	0.008	0.11	-
	CA -> Family support -> PI	0.01	0	3.08	0.002	0.02	14.2
	CA -> Friendship support -> PI	0	0	1.13	0.258	0.01	-
	Total -> PI	0.06	0.02	2.7	0.007	0.12	-
NSPN	CA -> Family support -> DS	0.03	0.01	5.89	< 0.001	0.1	29.5
	CA -> Friendship support -> DS	0.02	0	5.11	< 0.001	0.05	15.4
	Total ->DS	0.11	0.01	10.18	< 0.001	0.34	-
	CA -> Family support -> AEB	0	0	0.06	0.952	0	-
	CA -> Friendship support -> AEB	0.01	0	3.62	< 0.001	0.04	10.8
	Total -> AEB	0.04	0.01	6.37	< 0.001	0.25	-
	CA -> Family support -> PI	0.02	0.01	2.83	0.005	0.05	14.7
	CA -> Friendship support -> PI	0.02	0	6.32	< 0.001	0.07	20
	Total -> PI	0.1	0.01	10.67	< 0.001	0.32	-

Table 9.4: CA = Childhood adversity. DS = depressive symptoms. AEB = Anomalous Experiences & Beliefs. PI = Paranoid Ideation.

See Table 9.4 for results of indirect path estimation and mediation analyses. In ROOTS, the effect of CA promoting DS and PI, but not AEB, was partially mediated by worsening social support from family (16.5% CA->DS mediated, 14.6% CA->PI mediated).

In NSPN, the effects of CA promoting DS and PI was partly mediated by worsening support from

family (29.5% CA->DS mediated, 14.7% CA->PI mediated) and the effects of CA promoting DS, PI and AEB were partly mediated by worsening support from friendships (15.4% CA->DS mediated, 10.8% CA->AEB mediated, 20% CA->PI mediated).

9.5 Discussion

In this chapter, I showed that family-focused childhood adversity (CA) was associated with depressive/anxious symptoms (DS), anomalous experiences & beliefs (AEB) and paranoid ideation (PI), independently of any effects of recent social support and the relationships between CA and social support. Support from family and friends was a protective factor for DS and PI, but had less effect, if any, on AEB, suggesting dimensions of psychotic phenomena and distress are differentially sensitive to a positive recent social environment. In both cohorts, the association between CA and DS and PI were partly mediated by impairing perceived support from family later in life. In one cohort, CA was also associated with poorer support from friendships, which partly mediated the association between CA and all outcomes. A larger proportion of the CA associations with DS and PI were mediated by recent social support than the CA associations with AEB. Overall, these results suggest CA induces a long-lasting and potentially not-easily-modifiable predisposition towards unusual perceptual experiences and magical thinking. Compared to such phenomena, the manifestation of paranoia and depressive/anxious symptoms may be more influenced by the recent social environment. The implications of these results will be discussed in full in the next chapter.

This work has a number of strengths. These results were obtained, in-part, using prospective measurements and the substantive pattern replicated in two large general population cohorts of adolescents and young adults. Similar effects were observed whether CA was measured using a detailed care-giver interview or a self-report measure. Results were controlled for a large number of potential covariates.

This work is limited by retrospective assessment of CA, though this was partly mitigated in ROOTS by a detailed semi-structured interview method with timelines of adversities (Dunn et al., 2011). I considered CA broadly and did not investigate dissociable effects of specific types of adversities, such as indifference and abuse. Some adversities, such as sexual abuse, may predispose more strongly to psychosis than others, though findings in the literature are not fully consistent. It is therefore possible that the effects I found here could be driven by exposure to specific adversities and other effects of specific adversities could be obscured. Furthermore, abuse of any kind was fairly rare in the ROOTS cohort (Dunn et al., 2011). However, adversities tend to cluster (Dunn et al., 2011) so it may be ecologically valid to consider a general index of adversity severity. Further work might consider whether these effects are driven by specific adversity types. I considered only family-focused CA and did not include peer-focused adversities such as bullying, which are also associated with psychotic phenomena, psychopathology, and impaired social support. Further work will need to investigate peer-focused adversities in conjunction with family-focused adversities and social support. Though included as covariates, it is possible that there are age and/or sex differences in these pathways, such that overall effects were driven by heterogeneous effects across age or sex groups.

Chapter 10

Discussion: The social environment, psychotic experiences and psychopathology

10.1 Summary of findings

10.1.1 Question 4: How do PEs and social dispositions/social relationships influence one another over time?

In Chapter 8, I found that quality of recent social support and/or asocial dispositions discriminated phenotypes of PEs occurring with and without distress in young people (respectively: 'distressed, PE-prone', DPE; 'non-distressed, PE-prone', NDPE). These results could not speak to whether the association between the social environment and PEs was causal, in that social support might protect against distress or modify PEs, or whether the it was symptomatic, in that the underlying mechanisms driving PEs and distress would also impair social functioning. In this study, I made a step towards answering this question by investigating possible bidirectional longitudinal associations between social dispositions and dimensions of PEs in the NSPN cohort. Using cross-lagged structural equation modelling, I was able to infer that asociality unidirectionally predicted greater paranoid ideation (PI) and non-paranoid anomalous experiences and beliefs (AEB) one year later, with no evidence that either dimension of PEs predicted future asociality. This supported a temporal precedence in that social difficulties may precede or promote PEs. The effects of asociality on future PEs were mediated by effects on social support from family and friends, suggesting that asocial dispositions at one time predict later impairments in real world relationships that are associated with PEs. When I investigated associations between asociality and PE dimensions at one time with future markers of general mental health, I found that asociality and PI were predictive of depressive symptoms while asociality alone predicted future help-seeking for mental illness. Complementing the findings of clustering analyses, these results support a temporal precedence in which asociality precedes emergence or increase of positive psychotic phenomena.

10.1.2 Question 5: How are childhood adversity and social support related to one another and to later manifestation of distress and PEs?

In Chapter 8, I showed that the DPE and NDPE phenotypes were both associated with increased exposure to childhood adversity but were strongly differentiated by recent social support from family and friends. This raised the possibility that childhood adversity could predispose to some forms of PEs but paranoia and distress would be more strongly determined (or at least predicted by) recent social relationships and dispositions. Following the cluster analysis results in Chapter 7 and the association between the social environment and PEs evident in Chapter 9, I investigated longitudinal effects of childhood adversity and recent social support on later depressive symptoms and dimensions of PEs in both NSPN and ROOTS. Using structural equation modelling, I investigated, firstly, whether outcomes of depressive symptoms, AEB and PI were differentially influenced by childhood adversity or recent social support, as was suggested by the clustering analyses. Secondly, I tested whether any of the effects of childhood adversity on symptoms were mediated by impairing quality of supportive relationships later in life. Consistent with the symptom phenotypes returned by clustering, I found that childhood adversity, when considered without social support, predisposed to depressive symptoms, AEB and PI. These relationships remained with recent support from family and friends included in the model (though the association between adversity and PI in ROOTS fell to trend-level). In ROOTS, social support from family and friends both lowered depressive symptoms and PI, but not AEB. In NSPN, social support from family lowered depressive symptoms and PI, but not AEB, while support from friends lowered all three outcomes. In all cases, there was evidence that support lowered AEB less than it did PI or depressive symptoms. Mediation analyses showed that some, but not all of the effects of childhood adversity on depressive symptoms and PI was mediated by worsening later social support. In contrast, the effects of adversity on AEB were either not mediated or had smaller proportions mediated by social support. This was fully consistent with the results of clustering analyses, in that the NDPE group and DPE groups, who did not differ in terms of AEB but did in terms of depressive symptoms and PI, had similar exposure to childhood adversity but dramatically different levels of social support.

10.2 Discussion

10.2.1 Associations between the social environment, social functioning and psychosis: correlation or causality?

Together, these studies support the now well-evidenced association between childhood adversity and psychosis (Varese et al., 2012) and previous suggestions that adversity in early life predisposes to nonclinical as well as clinical PEs (Bebbington et al., 2004; Arseneault et al., 2011; Daalman et al., 2012). These studies also support the association between impaired social functioning/relationships and psychosis-proneness, further supporting that social difficulties precede onset or increase of psychotic phenomena (Jones et al., 1994; Monte et al., 2008; Strauss et al., 2012; Collip et al., 2013; Velthorst et al., 2016). My results further suggest some specificity of the associations between social support and dimensions of psychosis-proneness, in that positive

social relationships have greater protective effects against paranoid ideation than non-paranoid unusual perceptions and beliefs.

A key question to consider that arises from both of these studies is whether social difficulties are a cause or a correlate of the processes underlying positive psychotic phenomena. If both have a common underlying cause, the patterns observed here and elsewhere (Collip et al., 2013) of asociality promoting PEs and social support reducing paranoid ideation and depressive symptoms might reflect unfolding of a developmental process in which social behaviours are affected before subjective distortion of reality and associated distress.

Indeed, social impairments are well-known to precede and predict onset of clinical psychosis, being present both in children who go on to develop schizophrenia in adulthood (Jones et al., 1994; Malmberg et al., 1998) and becoming prominent before a first psychotic episode (Velthorst et al., 2016). My results show the same pattern occurring in subclinical variation in phenotypically similar traits. Social functioning may, therefore, be a valuable predictor of emerging psychotic experiences. Furthermore, social difficulties are far from specific to psychosis (Millan et al., 2012) and may transdiagnostically index risk and poor functioning (Caspi et al., 1996; Abbott et al., 2008).

My results, being observational, cannot distinguish between causality or common cause. If social difficulties have a causal role in promoting psychosis, then social networks and social dispositions may be suitable targets for reducing psychosis-proneness. Indeed, family and friendship-based interventions have shown some success at preventing relapse and minimising symptoms of psychotic illness (McFarlane et al., 2003; O'Brien et al., 2014; Poulton et al., 2014; Harrop et al., 2015). If impaired social functioning is an early manifestation of the psychopathological processes that later generate PEs, targeting social relationships themselves may not be effective but social functioning might still be a useful predictor of health trajectories.

Even if these associations were causal, I cannot infer whether these effects, namely asociality promoting PEs and social support reducing paranoid ideation and distress, are sufficient to drastically change someone's trajectories in terms of health and functioning. For example, improving social support may improve but not eliminate symptoms, or lessen the severity of first-episode psychosis but not prevent its occurrence.

10.2.2 Mechanisms by which the social environment may predispose to or protect against PEs and distress

At this point, I will discuss mechanisms by which the social environment may predispose to or protect against PEs and distress.

In Chapter 2, I described Marr's levels of analysis framework for investigations of information-processing functions (Marr, 1982). I described PEs in Marr's computational terms (the inputs, outputs and purpose of the computations performed) and introduced the predictive processing framework (Helmholtz, 1860; Lee and Mumford, 2003; Friston, 2005) that can be used to model them in algorithmic terms (fully describing the informational quantities and operations performed on them in order to achieve the process described at the computational level). In discussing

mechanisms of PEs and how the social environment may influence them, I will again appeal to this predictive processing framework (for further information, see Chapter 2).

Briefly, perception can be described as inferring properties of the environment (including bodily states) by integrating incoming sensory information, which is inherently ambiguous, with predictions from prior knowledge (Helmholtz, 1860). Prior knowledge can be modelled as a set of internal models that capture statistical regularities in the environment. These models track regularities over various spatiotemporal scales and across modalities and can be considered arranged in a hierarchy, ascending from low-level, unimodal sensory inputs to high-level, abstract beliefs (Mumford, 1992). In algorithmic terms, the most popular model of how inference can be achieved is by minimising the mismatch between predictions from internal models and incoming sensory input, which are termed prediction errors (Rao and Ballard, 1999; Friston, 2005). Within this model, predictions can be considered 'hypotheses' over the causes of sensory information and inference can be cast as testing hypotheses against reality (Gregory, 1980). Predictions will sometimes fail to match inputs because no internal models accurately capture the statistical properties of the environment that gave rise to those inputs. In these cases, prediction errors can be used to update internal models (Rescorla and Wagner, 1972; Pearce and Hall, 1980), changing the predictions they generate and thus learning about properties of the environment. Critically, the contribution of information sources (predictions & prediction errors) to inference and the degree to which they drive model updating should be weighted by their reliability (Knill and Pouget, 2004), so as to avoid learning inappropriately from unreliable evidence or wrongly inferring properties of the environment. Atypicalities in integration of stored prior knowledge with sensory information might cause aberrant inferences and learning, tending towards reality distortion (Fletcher and Frith, 2009; Adams et al., 2013; Jardri and Deneve, 2013).

Within this scheme, aetiological factors might predispose to or protect against PEs by disturbing the reliability-weighting of information sources, tending towards aberrant inferences and learning. In the remainder of this discussion, I aim to use this framework to map out possible pathways by which the social environment may influence PEs and by which different PEs may have different health implications. In doing so, I will discuss mechanisms proposed in the literature and attempt to expand on them by considering them in common computational terms. I consider the following non-exhaustive list of existing mechanisms by which the social environment (early life adversity and supportive social relationships) is theorised to influence PEs; the induction of negative affect, induction of cognitive biases (attentional biases and attributional biases), induction of maladaptive appraisals of experiences, attachment difficulties and dysregulation of the stress response. I also consider one more novel proposal; that the social environment influences the availability and use of information derived from other people in inference and learning.

Negative affect

Childhood adversity and poor social networks may predispose to PEs by induction of negative affect. Poor social support may also impair a normal buffer against stress and negative affect (Cohen and Wills, 1985). Affective dysregulation and negative affect commonly co-occur with psychotic symptoms and PEs, evident in the co-morbidity between emotional and psychotic disorders (Buckley et al., 2009) and the concurrence of depressive symptoms, anxious symptoms

and PEs in the general population (Stochl et al., 2015; van Nierop et al., 2015) (further supported in Chapter 7). In experience-sampling studies, increase in momentary negative affect preceded paranoid ideation (Kramer et al., 2014) and increase in anxiety or decrease in self-esteem preceded onset of paranoid episodes (Thewissen et al., 2011). The precise mechanisms by which negative affect might promote PEs are unclear. Emotional dysregulation may alter appraisals of the environment and experiences (Gross, 2002; Kramer et al., 2014) or may tend towards construction of negative schema and cognitive biases (Garety and Kuipers, 2001; Smith et al., 2006; Bentall and Fernyhough, 2008) (see below).

These mechanisms are difficult to model in computational terms because of limited understanding of the information-processing that underlies affect and how this relates to processes like perception. It could be that environmental influences like childhood adversity predispose to common computational changes manifesting as both emotional dysregulation and aberrant percepts/beliefs, or that one set of changes leads to the other. Negative affect may also be a correlate (even if temporally precedent) but not a cause of PEs or could be generated by PEs themselves.

Cognitive biases

Social environmental influences may predispose to PEs by promoting 'cognitive biases' (Bentall et al., 2001; Garety and Kuipers, 2001), a diverse set of phenomena denoting patterns of changes in information-processing.

Childhood adversity is associated with attentional biases towards threatening or emotional information, manifesting as rapid or preferential processing of threat-related or emotional stimuli in experimental tasks (Cisler et al., 2011; Wingenfeld et al., 2011), with similar biases evident in clinical psychosis (Besnier et al., 2011; Bendall et al., 2013) psychosis high-risk (Nieman et al., 2014) and PEs in the general population (Marks et al., 2012; Fisher et al., 2014). The effects of social support on attentional biases have, to my knowledge, not been investigated. These biases may be described in computational terms as effectively increasing the influence of emotionally-salient information on inference and learning. This could arise by increasing its availability through improved detection or increasing the weight afforded to it within a predictive processing scheme.

Childhood adversity is also associated with attributional biases, also referred to as attributional styles and closely related to theories on locus of control (Rotter, 1966). Psychosis is associated with an 'external' attributional style, in that events or experiences are more likely to be attributed to an external cause than an internal or self-generated one (Frenkel et al., 1995; Bentall and Fernyhough, 2008; Cooper et al., 2008; Thompson et al., 2011, 2013) and may mediate the association between childhood adversity and psychosis (Fisher et al., 2013). In computational terms, these attributional biases could be described themselves as internal models that act as priors for inference and learning, tending towards inferring external, rather than internal causes. This may result in incorrectly inferring causes of sensory data, tending towards unusual perceptions or interpretations of events.

Changes in the availability or use of socially-derived information

Information derived from others is critical to human success (Baldwin, 2000; Boyd et al., 2011), modulating learning even from infancy (Birch et al., 2008, 2010). Traditional learning models have tended to focus on information gained only from personal experience. However, information gained from observing and interacting with others alters our experience and beliefs about the world, ranging from low-level perceptual information (Sorkin et al., 2001; Bahrami et al., 2010; Campbell-Meiklejohn et al., 2012) to complex, high-level knowledge, like intentions and mental states (Kelley and Stahelski, 1970; Kilner et al., 2007; Kilner and Frith, 2008).

Asociality and impaired social relationships might cause aberrant or reduced use of socially-derived information, from implicit cues to explicit exchanges. Aberrantly interpreting socially-derived information may directly promote false inferences and inappropriate belief updating, like wrongly inferring the intentions of others. Under-using socially-derived information might allow aberrant beliefs to flourish by impairing a key mechanism of rejecting erroneous inferences: the guidance and opinions of others. This is especially important in the interpretation of social signals which are inherently uncertain, with this uncertainty only being resolvable through direct and cooperative interactions. Delusions are often about the intentions of others and the absence of a supportive social framework may rob the sufferer of an important information source.

Dysregulation of the stress response

The stress response comprises a set of physical and behavioural changes to allow an organism to meet environmental challenges or threats (McEwen, 2007; Koolhaas et al., 2011). The physiological parameters of the acute stress response are tightly tuned to environmental uncertainty and optimise learning when faced with uncertain threats (de Berker et al., 2016). This suggests that the stress response itself is determined by computation of environmental threat, with uncertain threats producing the greatest response.

The acute stress response then modulates inference and learning, with the goal, simplistically, being 'fight or flight'. Stress can directly influence perception (Simoens et al., 2007; Hoskin et al., 2014a, 2014b), favouring 'liberal' detection of signals (Hoskin et al., 2014a) (more detections at the cost of more false-positives), which might be adaptive when trying to detect threats. Stress modulates learning (Bogdan et al., 2011; Cavanagh et al., 2011; Radenbach et al., 2015), memory formation (Henckens et al., 2009; Schwabe and Wolf, 2010; Schwabe et al., 2012) and memory retrieval (Vedhara et al., 2000; Joëls et al., 2006), changing the way that internal models are updated and the information that might be accessed when next faced with a stressor. Stress may also lead to biased appraisals of events and information and over-generalization of learning about threats (Grillon et al., 2002; Lissek and Grillon, 2010), leading possibly to tenacious negative beliefs about the self, other people and the world (Garety and Kuipers, 2001; Smith et al., 2006; Fowler et al., 2012; Garety et al., 2013). It follows that acute stress precipitates PEs and depressive symptoms, by predisposing to false inferences (hallucinations), aberrant updating of internal models (formation of delusions or negative schema) and favouring using certain internal models to make sense of events (delusional or depressive appraisals).

Exposure to stressors and adversities early in life may predispose to PEs and depressive symp-

toms in adolescence and adulthood because they induce long-lasting dysregulation of the stress response, causing hyper-reactivity to stress and stress-related adaptations even in safe, predictable environments. Given that the physiological parameters of the stress response seems to be tuned to environmental uncertainty about negative outcomes (de Berker et al., 2016), dysregulation of the stress response might be considered dysregulation of the computation of uncertainty or the downstream effects of those computations. Failing to adapt to environmental uncertainty, such as by overestimating environmental volatility in preparedness for changes in contingencies, may result in aberrant inference and learning.

Disturbance to the computation of environmental threats could manifest physiologically, such as aberrant function of the hypothalamic-pituitary-adrenal axis, and psychologically, such as increased affective response to negative events. Neurobiologically, the increased stress reactivity that is evident in clinical psychosis and the extended psychosis phenotype, both psychologically (Myin-Germeys et al., 2001; Myin-Germeys and van Os, 2007) and physiologically (Aiello et al., 2012; Borges et al., 2013), could perturb brain processes underlying precise and accurate inferences about the world. Notably, dysregulation of the hypothalamic-pituitary axis may lead to aberrant prediction error signalling through dysregulation of dopaminergic neurons (Lodge and Grace, 2011; Grace, 2012).

Disturbance to computations of environmental uncertainty might arise from tonic exposure to uncertain, stressful environments. Importantly, volatility or inconsistency is a feature of adverse family environments (Goodyer et al., 2010). In a later chapter, I was able to directly investigate the influence of the social environment on associative learning and the modulation of behaviour by environmental volatility, testing whether there were any common computational correlates of the social environment and dimensions of PEs and distress.

Maladaptive appraisals of and responses to anomalous experiences

Returning to other mechanisms by which the social environment might influence PEs, the final mechanism I consider is that childhood adversity or social support may influence the appraisals of unusual experiences. Maladaptive appraisals and response styles are negative interpretations and behavioural responses to aberrant, psychotic-like experiences, such as forming a delusional belief about the origin of a hallucination. Maladaptive appraisals and response styles are considered central in cognitive models of the positive symptoms of psychosis (Chadwick and Birchwood, 1994; Garety and Kuipers, 2001; Morrison, 2001). The forming of maladaptive beliefs and behaviours around psychotic-like phenomena may be a critical factor that distinguishes clinical from nonclinical PEs. When compared to clinical PEs, nonclinical PEs are more associated with normalising appraisals that consider them within the realms of normative experience, less associated with externalising appraisals that infer them arising from an external cause (Brett et al., 2007; Lovatt et al., 2010; Peters et al., 2012) and less preoccupying and distressing (Lincoln, 2007; Sisti et al., 2012). More recently, the importance of appraisals has been supported by studies investigating how they shape the impact of experimentally-induced anomalous experiences, finding that adaptive appraisals reduce the distress of phenomena that model some aspects of PEs (Taylor et al., 2013; Ward et al., 2014; Underwood et al., 2016). This is consistent with theoretical work arguing that delusions 'complicate' perceptual dysfunction (Maher, 1974) and

further supported by epidemiological evidence that PEs may progress towards clinical relevance as anomalous perceptions become compounded by anomalous, delusion-like beliefs (Smeets et al., 2012a, 2012b, 2014).

Childhood adversity and poor social support may both tend towards maladaptive appraisals. This could be through an 'affective route', by inducing negative affect or predisposing to negative beliefs about the self, others and the world that supply content for the formation of maladaptive appraisals (Garety and Kuipers, 2001). Both could also disturb the computations that underlie the appraisals of experiences in a mechanism, potentially independent of affect, that tends towards bizarre or unusual appraisals. Given that appraisals and PEs themselves can be considered as arising from similar disturbances within a predictive processing hierarchy, bizarre appraisals may arise from the same mechanisms that generate bizarre experiences. Social support may have a greater influence on paranoia than other PEs by acting on the appraisals of psychotic phenomena, rather than their occurrence.

Theoretical and empirical work on maladaptive appraisals suggests that anomalous beliefs may be more maladaptive than anomalous perceptions (supported by results of clustering analyses in Chapter 7) and that reality distortion in clinical psychosis may arise as delusions are formed around anomalous experiences. Critically, both anomalous perceptions and beliefs can be considered in terms of atypicalities in information-processing within a predictive processing framework. Despite their above-chance co-occurrence (Smeets et al., 2012b), the differential clinical implications and aetiological associations (supported by Chapter 9) of anomalous perceptions and anomalous beliefs suggests they may have partly distinct computational mechanisms.

10.3 Further Questions

Based on the results from previous chapters, I devised two final questions that centred on the computational mechanisms of PEs.

10.3.1 Are PEs in adolescents associated with reduced modulation of behaviour by confidence? Could this be induced by exposure to childhood adversity early in life?

The early development of psychosis is sometimes characterised by a pervasive sense of uncertainty and the feeling that the world has changed. This might arise from disruption to how confidence modulates behaviour and experience. In a recent study, Vinkcier et al. (2016) reported that subanaesthetic administration of ketamine, a pharmacological model of psychosis, impaired the ability of healthy volunteers to use confidence in knowledge about the environment to shape their behaviour. I planned to investigate whether a similar reduction in the modulation of behaviour by confidence was associated with PEs in adolescents, using computational modelling of behavioural data from the ROOTS cognition sub-study (see Methodology). This might shed light on computational mechanisms by which PEs arise, complementing and extending the results of Vinckier et al. (2016).

Atypicalities in how confidence is used to modulate behaviour might arise as a result of chronic

exposure to volatile, unpredictable and hazardous environments. Volatility is a common component of adverse family-environments (Dunn et al., 2011). It is therefore plausible that exposure to childhood adversity might cause long-lasting changes in the use of confidence that predispose to PEs. If so, this would represent rare evidence of the computational mechanisms by which an environmental risk factor might cause PEs. I thus also investigated whether childhood adversity was associated with atypical modulation of behaviour by confidence.

10.3.2 What are the computational mechanisms by which anomalous perceptions and beliefs arise?

PEs might arise from aberrant integration of sensory evidence and prior knowledge in perceptual inference and belief updating (Fletcher and Frith, 2009) (see Review II). However, there is suggestion of over-reliance on predictions (Behrendt, 1998; Aleman et al., 2003; Corlett et al., 2009; Teufel et al., 2015) or weak prediction errors (Horga et al., 2014), deficits generating or using predictions (Hong et al., 2005, 2008; Shergill et al., 2005; Umbricht and Krljes, 2005) and complex hierarchical interactions between changes in reliability of sensory evidence and higher beliefs (Schmack et al., 2013). This is complicated by lack of translation of findings across clinical psychosis and nonclinical PEs. Teufel et al (2015) (Teufel et al., 2015) found increased ability to use prior knowledge in perceptual inference in both psychosis high-risk and psychosis-proneness in healthy volunteers. I planned to replicate and extend their findings in a nonclinical sample by investigating whether the reliance and the information content of predictions in perceptual inference varied with psychosis-proneness, using a novel experimental task with computational modelling of reaction times.

Chapter 11

Psychotic experiences in adolescents are associated with a reduction in the modulation of learning by confidence

Abstract

Psychosis might arise from impairments in weighting the reliability of information sources. This could generate pathological uncertainty, or a lack of confidence in knowledge of the world, rendering a person susceptible to distortion of reality. Over-estimation of environmental uncertainty might arise from exposure to volatile, unpredictable environments, such as can characterise childhood adversity, a known risk factor for psychosis. Using a reinforcement learning task, I investigated whether psychotic experiences and childhood adversity were associated with reduced modulation of behaviour by confidence in learned environmental contingencies. Data came from a sub-set of 250 participants from a general population sample of adolescents (ROOTS). Around half the participants had experienced a form of childhood adversity. The task required participants to learn about and choose between stimuli. Uncertainty was modulated on two levels: feedback was sometimes unreliable and the reward contingencies reversed half-way through. Bayesian model selection of a family of computational models fit to trial-by-trial behaviour confirmed that participants modulated learning according to confidence in learned contingencies, an adaptive mechanism that prevented learning from contradictory feedback when the environment was stable. Increases in the severity of non-paranoid unusual perceptions and beliefs correlated with lower modulation of learning by confidence. In simulations, reducing this modulation parameter allowed quicker adaptation of behaviour to contingency reversal, suggesting it may be an adaptation to volatile environment, but came at the cost of increased switching of responses when contingencies should be well-known. This was very similar to recent findings on the computational effects of ketamine in healthy volunteers, suggesting convergent mechanisms with a pharmacological model of early psychosis. However, there were no associations between behaviour in the task and childhood adversity. While its aetiology remains unclear, atypicalities in how confidence is used to guide behaviour may be a critical step in the development of psychosis.

11.1 Research Questions

- Are PEs in adolescents associated with reduced modulation of behaviour by confidence?
- Could this be induced by exposure to childhood adversity early in life?

11.2 Introduction

Early clinical psychosis often features a pervasive sense of uncertainty and the feeling that the world, or one's perception of it, has changed or become strange (Cutting and Dunne, 1989; Kapur, 2003). This is sometimes associated with motivation to understand what has changed and why, leading possibly to bizarre behaviours, finding meaning in meaningless events or forming bizarre, unfounded beliefs. As Peter Chadwick writes about his own psychotic episode, accompanying the disturbances to his thoughts and perceptions was the sense that he "[had] to see where all this leads." (Chadwick, 2007).

Uncertainty in knowledge about the world may be a manifestation of the atypicalities in information-processing that cause early psychotic experiences (PEs). Current models based on the predictive processing framework posit that PEs might arise from atypicalities in the estimation of reliability of information sources in perceptual inference and belief-updating (Fletcher and Frith, 2009; Adams et al., 2013). In deriving properties of the environment and learning from unreliable evidence, perceptions and beliefs might diverge from consensus reality.

The predictive processing framework posits that the brain derives properties of the environment and determines behaviour by integrating prior knowledge with current inputs collected via the senses (for review, see Clark, 2013). Prior knowledge may be encoded as a set of internal generative models that describe statistical regularities in the environment. Internal models can specify statistical regularities in different types of information and over different spatial and temporal scales. Internal models are arranged in a hierarchy, increasing in complexity and in abstraction from sensory input through to abstract, high-level beliefs (Mumford, 1992). Predictions from these models, akin to hypotheses (Gregory, 1980), are compared to inputs and any mismatch between them is termed prediction error. By finding predictions that minimise prediction errors, the brain can optimally derive properties of the environment (Helmholtz, 1860; Lee and Mumford, 2003). Sometimes, prediction errors reflect that models do not optimally capture environmental regularities. In these cases, predictions can drive learning: the updating of internal models (Rescorla and Wagner, 1972; Pearce and Hall, 1980). This may form a kind of canonical computation used by the brain (Friston, 2005). Critically, the brain must differentiate prediction errors that signal when an internal model poorly represents the environment and needs updating versus those that are meaningless, such as arising from randomness. It may do this by weighting its information sources (internal models and incoming information) by their reliabilities (Knill and Pouget, 2004), such that mismatch between inputs and predictions is ignored when internal models are highly reliable or current inputs are unreliable. Conversely, when predictions are unreliable or current inputs very reliable, internal models may be readily updated. Reliability itself is something that the brain must estimate and encode.

Atypicalities in the estimation or signalling of reliability might cause aberrant model updating and inference, tending towards distortion of beliefs and percepts (Fletcher and Frith, 2009; Adams et al., 2013). It might also manifest subjectively as a pervasive uncertainty or loss of confidence (here treated simplistically as the inverse of uncertainty) in knowledge of the world. Confidence might be intrinsically related to estimations of the reliability of internal models, or how well they can predict the environment. We can frame this in tractable computational terms by thinking of how high and low confidence in models of the world might shape behaviour. Vinckier et al., (2016) describe a computational treatise of confidence as a form of 'meta-learning' that tracks the reliability of internal models and shapes behaviour in two possible ways. Firstly, confidence might modulate model updating to update less from contradictory evidence and update more from confirmatory evidence, as a kind of computational implementation of 'confirmation bias'. Secondly, confidence might change how informational values are transformed into behaviour by making actions more deterministic, rather than exploratory, allowing people to exploit learned contingencies. Failure to utilise confidence in the first sense might lead to model updating from contradictory evidence even when contingencies are stable, rendering beliefs inappropriately malleable even when well-supported and a feeling that the world is strange or unfamiliar. Failure to utilise confidence in the second sense might cause odd or bizarre behaviours that make little sense to observers or perhaps even the actor themselves.

By formalising this theory of confidence in a generative mathematical model, Vinckier and colleague showed that this model better explained the behaviour of participants in a behavioural task in which uncertainty was experimentally manipulated, compared to simpler models without any meta-learning confidence features. The authors then showed that administering subanaesthetic ketamine, a pharmacological agent thought to mimic some features of early psychosis, reduced the modulation of learning and of action selection by confidence in healthy volunteers, supporting atypicalities in the estimation or utilisation of confidence being associated with PEs. The authors also mapped this onto specific neural substrates. In this chapter, I set out to extend these findings by testing whether psychotic experiences (PEs) in adolescents were associated with a similar reduction in confidence modulation using computational modelling of behaviour. If so, this would provide evidence for a common computational mechanism underlying both PEs in the general population without psychotic disorders and a pharmacological model that can induce psychotic-like phenomena.

Estimating one's confidence in internal models might itself be a process that is influenced by experience. Exposure to volatile and unpredictable adverse environments during critical developmental periods like childhood and adolescence may cause persistent expectations of volatile environments in the future and low confidence in internal models, effectively impairing the tuning of confidence to environmental stability. Volatility in childhood environments, such as through unreliable relationships or attachments, can be harmful, forming a component of childhood trauma (Dunn et al., 2011). People exposed to childhood adversity (CA) may modulate their behaviour by confidence less, as an adaptation to be ready for sudden environmental changes. CA predisposes to psychosis (Varese et al., 2012), supported by results in earlier chapters of this thesis. Reduction in the confidence-modulation of behaviour could therefore be a mechanism by which CA causes PEs. Accordingly, I also investigated whether exposure to childhood adversity was associated with reduced modulation of behaviour by confidence.

11.3 Methods

11.3.1 Data

A subset of 277 ROOTS participants performed a contingency learning task as part of a battery of cognitive tasks during an additional in-unit assessment. The study took place between time 2 and time 3 of the ROOTS study. The sample was recruited using opportunistic sampling within the larger ROOTS cohort, enriched for exposure to CA and for variants of the 5-HTTPLR (Owens et al., 2012), the main focuses of the original study. Complete trial-by-trial data was available for 250 participants.

11.3.2 Psychotic experiences

Dimensional symptom phenotypes were measured at age 17. The self-report Brief Schizotypal Symptoms Inventory (BSSI) measured state PEs occurring over the previous two weeks in two dimensions: Anomalous Experiences & Beliefs (AEB), comprising unusual perceptual experiences and magical thinking, and Paranoid Ideation (PI), comprising ideas of reference and suspiciousness. 198 participants had complete data on the task and the BSSI instruments.

11.3.3 Childhood adversity between ages 0-14

CA was measured between ages 0-14. Childhood adversity between 0-14 years was measured using a detailed caregiver interview, the Cambridge Early Experiences Interview (CAMEEI), at age 14. The CAMEEI was mostly performed with biological mothers (96%). Inter-rater reliability on a subset of interviews was high, with kappa ranging between 0.7-0.9. I calculated a sum score of the number of adversities (family death/separation, moderate/severe family discord, abuse (physical/sexual/emotional), family criminality, financial problems and unemployment, maternal psychiatric illness, paternal psychiatric illness, aberrant parenting styles (either parent) and lack of maternal affection/engagement) experienced in this period. 193 of the participants had complete data on the task and the CAMEEI.

11.3.4 Contingency learning task

The contingency learning task required participants to choose between two stimuli, one of which was correct and one incorrect. The task comprised 80 trials. On every trial, participants chose one stimulus by touching it. They received probabilistic feedback after every choice. The correct stimulus was reinforced with an 80:20 positive/negative feedback ratio, respectively. The incorrect stimulus was reinforced with a 20:80 positive/negative feedback ratio, respectively. After 40 trials, the identities and feedback ratios of the correct and incorrect stimuli reversed. Participants were not informed that there would be a reversal.

Instructions to participants were:

"On each go, the same two patterns will be presented. One of the patterns is correct and the other pattern is wrong and you have to choose the correct pattern on each go. However, on some goes,

Figure 11.1: Response switching and perseverative errors

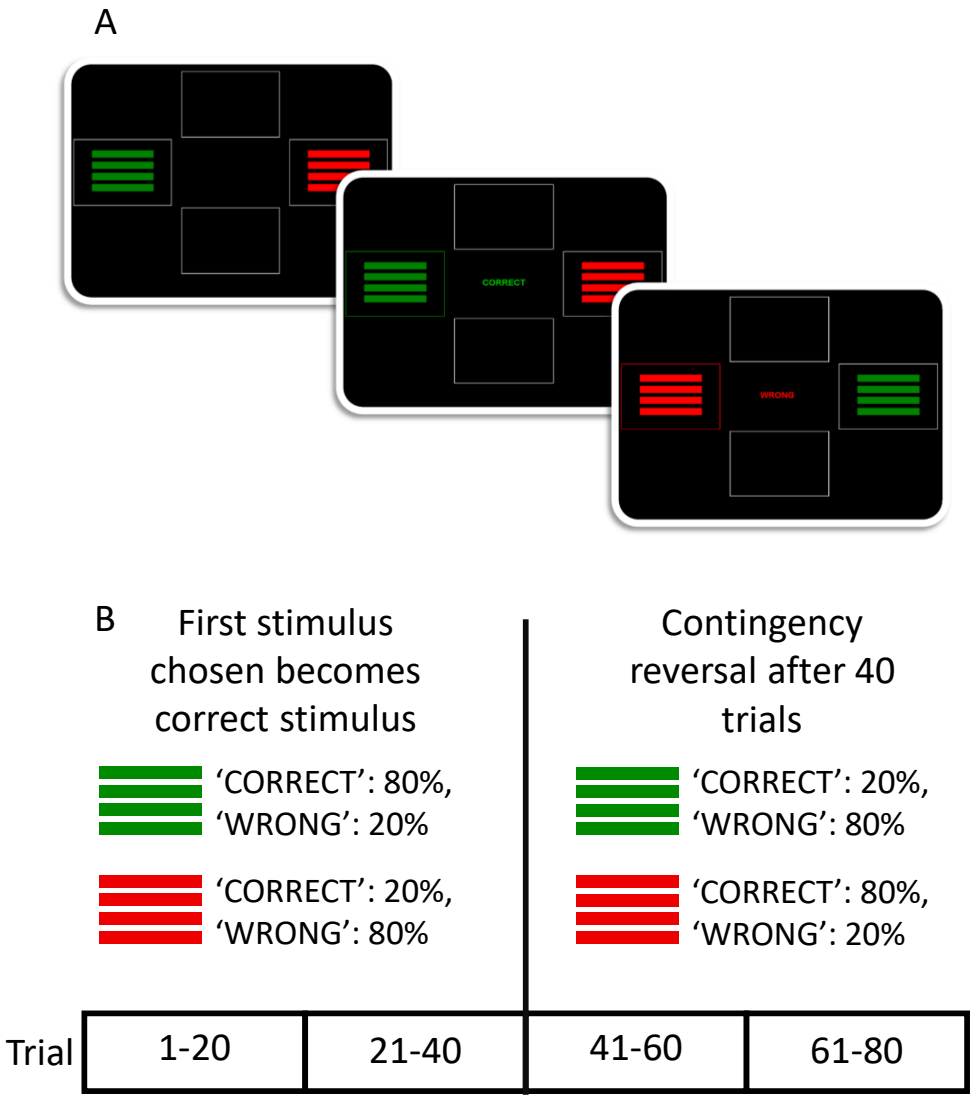


Figure 11.1: A) Example of task screen. Participants chose between two stimuli on every trial by touching them on a tablet computer. B) The first stimulus chosen became the 'correct' stimulus for the first half of the experiment. Uncertainty was introduced at one level by sometimes giving misleading feedback: the correct stimulus was followed by a 'correct' message 80% of the time and a 'wrong' message 20% of the time. The 'incorrect' stimulus had the opposite reward contingences. Further uncertainty was introduced after 40 trials when these contingencies reversed.

the computer will tell you that you were wrong even if you chose the correct pattern. Your task is to stick to the pattern that is usually correct. So in other words always choose the pattern that is correct more often than the other pattern."

The first stimulus that the participant chose became the correct stimulus for the first block. Stimuli consisted of four red or four green horizontal lines. The task was performed on a touchscreen tablet and participants chose stimuli by touching them.

11.3.5 Model-free behavioural analyses

I investigated two model-free behavioural measures of performance: switches and perseverative errors after reversal. Switches were defined as choosing a different stimulus to the previous trial. Perseverative errors were defined as choosing the poor stimulus on two consecutive trials. I calculated these performance measures over sets of 20 trials, to capture early pre-reversal behaviour, late pre-reversal behaviour, early post-reversal behaviour and late post-reversal behaviour. Relationships between PEs, CA and behaviour were tested using Kendall's tau correlations.

11.3.6 Computational model-based analyses

I also fit reinforcement learning computational models to the trial-by-trial data. Following the analysis by Vinckier et al., (2016), I fit simple Q-learning models (Sutton and Barto, 1998) as a baseline and progressively extended them with parameters representing confidence and its influence on behaviour.

In all models, the value of a cue (c) for a given trial, t, according to the delta rule:

$$Q_c(t+1) = Q_c(t) + \alpha\delta(t)$$

where α is a free 'learning rate' parameter ($0 \leq \alpha \leq 1$) that determines the degree of Q-value updating and δ(t) is the prediction error, or the difference between actual and expected outcome:

$$\delta(t) = R_c(t) - Q_c(t)$$

where *R(t)* is the actual reward. Feedback was either 'correct' or 'incorrect', so R was either 1 or -1.

The probability of choosing a particular stimulus was estimated from the expected value of the stimulus according to the softmax rule:

$$P_c(t) = \frac{1}{1 + e^{\frac{Q_c(t)}{\beta}}}$$

where β is a free parameter of 'choice temperature' (β>0). β modulates the degree of exploration of choices, as opposed to exploitation of the learned value.

In the simplest model, the Q-value for a stimulus was only updated if that stimulus was chosen, so the model treated the Q-values as independent. In a second variant, the Q-values for each stimulus (1 or 2) were updated symmetrically, such that:

$$Q_1(t) = -Q_2(t)$$

In a third variant a single prediction error value was calculated, depending on the action chosen, and the Q-values updated by the same amount in opposite directions, such that if stimulus 1 were chosen (and vice versa for stimulus 2):

$$\delta(t) = R_1(t) - Q_1(t)$$

$$Q_1(t+1) = Q_1(t) + \alpha\delta(t)$$

$$Q_2(t+1) = Q_2(t) - \alpha\delta(t)$$

The initial Q-values were fit as free parameters that were allowed to differ. The third model variants preserved initial differences between Q-values.

In a further set of models, an additional parameter that tracked trial-by-trial confidence was added that could modulate the learning rate and choice temperature parameters. Traditional reinforcement learning models treat parameters as constant over all trials, limiting optimisation of behaviour when participants have good knowledge of contingencies. Modulating parameters using confidence allowed optimisation of behaviour in late pre-reversal and late post-reversal trials, when values should be well-established and participants would be able to exploit learned contingencies.

Confidence (C) was updated using a delta rule:

$$C(t+1) = C(t) + \gamma(O(t) - C(t)$$

where γ is a confidence learning rate parameter ($0 \leq \gamma \leq 1$) and O(t) is the outcome (either correct feedback, 1, or incorrect feedback, -1).

There were four variants on how confidence modulated reinforcement learning: confidence could modulate learning rate, choice temperature, learning rate and choice temperature with different weights, or learning rate and choice temperature with equal weights.

Learning rate was modulated differently for confirmatory outcomes, when observed outcomes were of the sign predicted by Q-values, and contradictory outcomes, when observed outcomes were in the opposite sign to predictions from Q-values.

For confirmatory outcomes, modulated learning rate (αm) was calculated as follows:

$$\alpha m(t) = \frac{\alpha 0 + k_\alpha C(t)}{1 + + k_\alpha C(t)}$$

where $\alpha 0$ is the initial learning rate and k_α is the modulation weight for learning rate.

For contradictory outcomes, learning rate was modulated as follows:

$$\alpha m(t) = \frac{\alpha 0}{1 + + k_\alpha C(t)}$$

Learning rate therefore became closer to 1 for confirmatory outcomes and closer to 0 for contradictory outcomes.

Choice temperature was modulated (βm) as follows:

$$\alpha m(t) = \frac{\beta 0}{1 + + k_\beta C(t)}$$

where $\beta 0$ is the initial choice temperature and k_β is the modulation weight for choice temperature. As confidence increased, choice temperature reduced such that behaviour became more deterministic, allowing participants to exploit learned contingencies.

The full model space comprised 15 models: all combinations of 3 variants of Q-value updating:

- single value updated
- symmetrical update with no initial difference
- symmetrical update with free initial difference

and 5 variants of using confidence to modulate behaviour:

- no modulation
- modulates α
- modulates β
- modulates α & β with different weights
- modulates α & β with equal weights

11.3.7 Model fitting

All models were fit using the VBA toolbox (Daunizeau et al., 2014), which inverts models using a variational Bayes approach under the Laplace approximation, which inverts nonlinear models and estimates their 'evidence': a trade-off between goodness of fit and complexity (Stephan et al., 2009). I used random-effects Bayesian model selection to identify the best fitting model overall, indicated by the model log-evidence and exceedance probability (Rigoux et al., 2014). Finally, I used family-wise analyses to test whether particular modifications changed model performance.

Parameter estimates from the winning model were calculated for each subject. Associations were tested between model parameters and dimensions of the social environment and symptom phenotypes that showed associations with task performance in model-free analyses. The distributions of social environment and symptom phenotype scores were likely to be highly skewed and feature tied-values, so I tested associations using Kendall's tau correlations.

Model parameters are not meaningful when a model poorly explains subject behaviour. I tested whether the winning model performed above chance for each participant by comparing the log-evidences of the winning model and a model that made random choices. A difference in log-

Figure 11.2: Response switching and perseverative errors

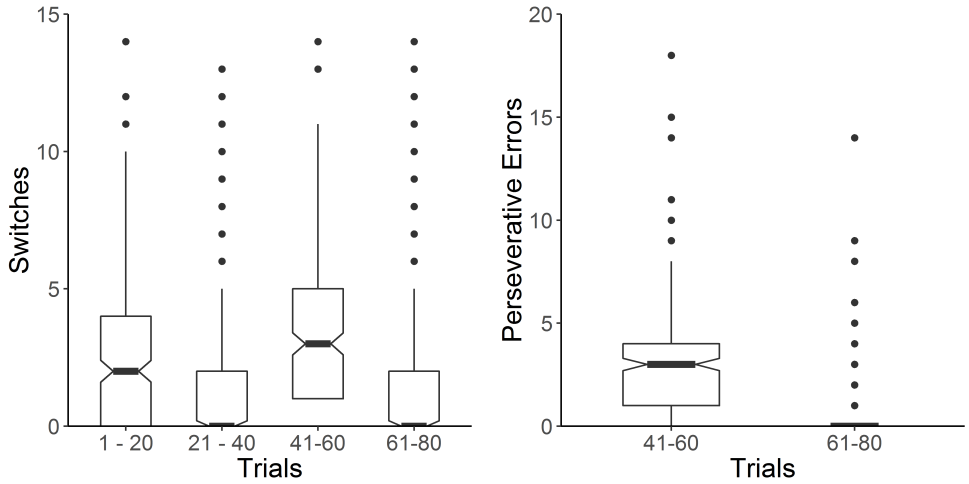


Figure 11.2: Response switching, defined as changing response from the previous choice, and perseverative errors, defined as two consecutive choices of the poor stimulus after contingency reversal. Reversal occurred at trial 40. Thick line = median. Hinges = interquartile range. Whisker = 1.5x interquartile range from hinge.

evidence of 3 (approximately equal to a Bayes Factor of 20) indicates better-than-chance performance. I also calculated predictive validity of the models, in terms of behavioural variability explained (r^2). Finally, I tested whether any effects could be driven by model fit systematically changing with social/symptom variables by testing their correlation with r^2.

11.4 Results

11.4.1 Model-free behavioural analyses

Participants made different numbers of switches across the blocks (Figure 11.2), confirmed by heteroskedastic one-way ANOVA for 20% trimmed means ($F_{(3,\ 327.87)} = 30.54$, $p < 0.001$). Pairwise comparisons showed the mean number of switches varied across all sets of trials ($p_{Holm}<0.001$) other than the second and fourth sets, consistent with participants making few switches once contingencies have been stable for some time.

Participants made more perseverative errors in the first 20 post-reversal trials than the second 20 post-reversal trials, confirmed by Yuen's t-test for 20% trimmed means ($t = 19.17$, $df = 149$, $p < 0.001$).

AEB were associated with increased response switching in the first and last sets of 20 trials (Trials 1-20: $\tau = 0.14$, $p = 0.02$; Trials 61-80: $\tau = 0.13$, $p = 0.04$), which might reflect failure to adapt to stable contingencies. AEB were also associated with making more perseverative errors in the first 20 post-reversal trials ($\tau = 0.12$, $p = 0.03$) but not the second set, suggesting difficulty detecting the change in contingencies. Neither PI nor CA were associated with switching or perseverative errors in any set of trials. Given their lack of behavioural associations, I did not investigate associations between CA and PI in model-based analyses.

11.4.2 Computational model selection

Bayesian model selection confirmed that the best fitting model was the model with dual updating of Q-values by a single prediction error in which confidence modulated learning rate (Figure 11.3, exceedance probability for winning model = 1). Family-wise analyses supported use of both of these features: symmetrical updating of Q-values with no difference in initial Q-values other Q-value updating variants (exceedance probability = 1) and confidence modulation of alpha outperformed other confidence modulation variants (exceedance probability = 1). The model fit better than chance in 235 out of 250 participants. Variability in behavioural choices was well-explained by the model (r^2: median = 0.96, mad = 0.90 – 0.99).

11.4.3 Association of model parameters with PEs

I calculated parameter estimates for the 235 participants whose behaviour was well-explained by the model. In keeping with my hypothesis, confidence modulation weight (κ) correlated negatively with AEB (τ = -0.16, p = 0.001).

In post-hoc analyses, I tested associations between AEB and other parameters of the model. AEB was associated with higher base learning rate ($\tau = 0.15$, p = 0.003) and higher choice temperature ($\tau = 0.11$, p = 0.03). AEB was therefore associated with increased learning rate, more exploratory behaviour and reduced modulation of learning rate for contradictory and confirmatory evidence when contingencies were well-known.

To test whether reduced modulation of learning rate by confidence could account for any of the behavioural atypicalities associated with AEB, I used the model to simulate responses with varying modulation weight but holding other parameters constant. Modulation weight took 5 possible values (the 5th, 25th, 50th, 75th and 95th sample percentiles) while all other parameters were fixed to the median. The same reward schedule as the main task was used. 200 datasets with 80 trials were simulated per level of confidence modulation, generating 1000 datasets in total.

Reduced modulation of learning rate by confidence predicted more switching in trials 61-80 (τ = 0.05, p $<$ 0.001), replicating behavioural changes associated with AEB. It did not predict switching in the first set of 20 trials but predicted more switching in trials 21-40 (τ = 0.02, p = 0.01) and trials 41-60 (τ = 0.06, p $<$ 0.001). In contrast to the associations with AEB, reduced modulation of learning rate by confidence was associated with fewer perseverative errors in the trials 41-60 (τ = -0.09, p $<$ 0.001) and 61-80 (τ = -0.05, p $<$ 0.001). Reducing the modulation of learning by confidence thus reproduced one aspect of the behavioural associations of AEB but had more complex effects on other aspects of behaviour. Interestingly, reduced modulation of learning tended towards greater switching through most of the task but led to fewer perseverative errors, suggesting it may be adaptive in volatile environments but maladaptive in stable environments. Varying this parameter alone therefore did not reproduce all behavioural associations of AEB.

Figure 11.3: Bayesian model comparison

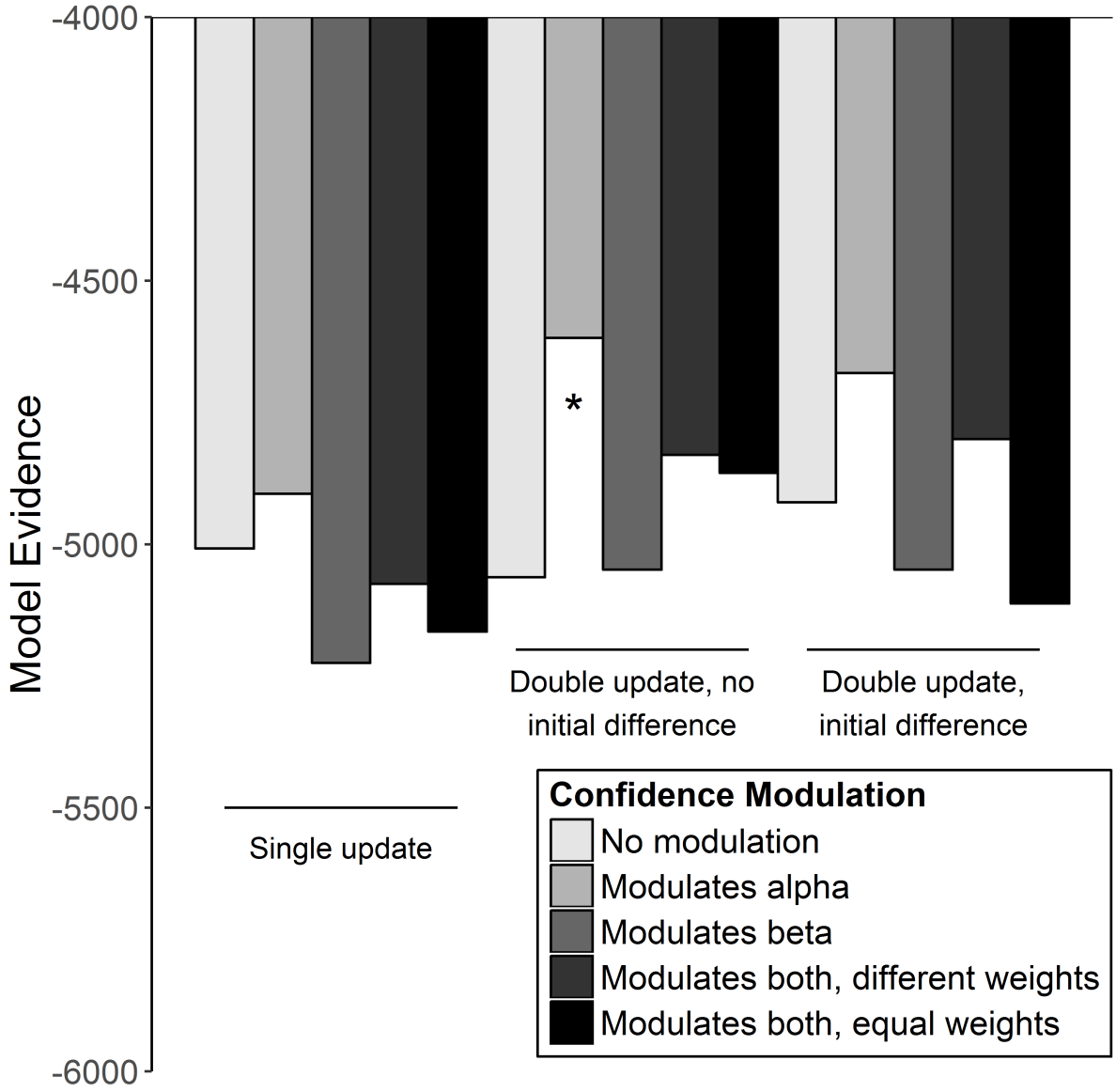


Figure 11.3: Bayesian model comparison favoured a model with symmetrical updating on every trial and with no initial difference in Q-values (marked with *). The exceedance probability of this model was 1.

11.5 Discussion

In this chapter, using data from a sub-set of 250 participants from ROOTS, I investigated whether PEs were associated with reduced modulation of behaviour by confidence in knowledge of the environment and whether this might arise as a result of exposure to volatile, adverse environments in childhood. Around half the participants had experienced a form of childhood adversity. The task required participants to learn about and choose between stimuli using unreliable feedback and reward contingencies reversed half-way through. Bayesian model selection of a family of computational models fit to trial-by-trial behaviour confirmed that participants modulated learning according to confidence in learned contingencies, an adaptive mechanism that prevented learning from contradictory feedback when the environment was stable. Increases in the severity of non-paranoid unusual perceptions and beliefs correlated with lower modulation of learning by confidence. In simulations, reducing this modulation parameter allowed quicker adaptation of behaviour to contingency reversal, suggesting it may be an adaptation to volatile environment, but came at the cost of increased switching of responses when contingencies should be well-known. However, there were no associations between behaviour in the task and childhood adversity. While its aetiology remains unclear, atypicalities in how confidence is used to guide behaviour may be a critical step in the development of psychosis.

Failing to down-weight learning from prediction errors when environmental contingencies are stable and well-known could effectively induce persistent uncertainty about learned associations (Vinckier et al., 2016) and induce inappropriate learning from events. In this task, that took the form of greater updating of the expected values of stimuli, even when those values were well-known and feedback was sometimes unreliable. In ecological conditions, this may tend towards an excessive influence of prediction errors, even those arising from predictions from internal models that can reliably predict the environment. The result may be destabilisation of internal models and the predictions they make. This could subjectively manifest in the pervasive sense of uncertainty that often accompanies early psychotic symptoms (Kapur, 2003; Micoulaud-Franchi et al., 2012). In a previous study, modulation of learning parameters by confidence was shown to be reduced by ketamine administration in healthy volunteers using a similar learning task (Vinckier et al., 2016). This is therefore evidence for a common computational mechanism that links variation in a specific dimension of psychosis-proneness and a pharmacological model of psychosis. Based on the results of this study and of Vinckier et al. (2016), I argue that reduction in the modulation of learning by confidence could therefore be a causal mechanism for some PEs.

It is important to emphasise that most participants in this study were not developing the early stages of clinical psychosis. Indeed, none of them might have gone on to have a psychotic disorder. These results therefore suggest that reduced modulation of learning by confidence is associated with nonclinical PEs distributed in the general population and, while these findings generate hypotheses about clinical psychosis, they tell us nothing about it directly. Furthermore, we do not have direct measurements of a pervasive sense of uncertainty.

I also note that the concept of pathological uncertainty driving development of psychosis might seem at odds with the fact that clinical psychosis is associated with fixed, bizarre and over-valued ideas and beliefs, like delusions. If people prone to PEs do not modulate their learning

by confidence, why then do these anomalous beliefs persist, as opposed to being continuously updated? We might shed some light on this problem by appealing to the hierarchical nature of predictive processing (Mumford, 1992). Reduction in how confidence shapes behaviour at one level of the hierarchy may coincide with, or even drive, opposing increases in confidence in internal models at other levels. Specifically, uncertainty at lower-hierarchical levels may tend towards over-relying on high-level internal models encoding abstract beliefs. A recent study showed experimental support for this in a general population sample. Schmack et al. (2013) tested hierarchical influences of expectations on perceptual inference and found that delusional ideation was associated with instability of low-level percepts but a greater ability to stabilise percepts using abstract beliefs. Psychosis and PEs may therefore not represent single, unitary deficits such as 'impaired ability to use confidence to shape behaviour' but probably arise from complex interactions of and compensations for perturbations to information-processing.

In particular, thinking about psychosis in this way might let us speculate on the mechanisms of the transition from early stages of psychotic symptoms to full-blown psychotic illness. I predicted that PEs, like ketamine, would be associated with a *reduction* in how confidence shaped behaviour. Reduced confidence-modulation might then allow beliefs to be updated from evidence that would otherwise be ignored, rendering internal models overly malleable. However, the transition to clinical psychosis may be associated with a shift in the opposite direction, such that confidence in some internal models is estimated as inappropriately high. Excess confidence may bestow predictions with undue influence on behaviour and experience and negate any contradictory evidence against the models that generated them. This effect may not be general for all predictions: when repeating the paradigm of Schmack et al. (2013) in patients with chronic schizophrenia, Schmack et al (2017) found that the influence of beliefs on perception was *lower* than a healthy control group, but the influence of beliefs within the patient group correlated with positive symptoms. The authors interpreted this as a weaker acquisition of externally-generated beliefs and a compensatory increase in the influence of predictions on perception (Schmack et al., 2017). This might be consistent with the entrenchment and over-weighting of a subset of maladaptive internal models that suppress prediction error, inhibiting acquisition of new beliefs but strengthening the influence of beliefs once acquired.

Returning to Chadwick's first-hand account of a psychotic episode, he writes: "Another way of putting things was that confirmation bias was massively amplified, everything confirmed and fitted the delusion, nothing discredited it. Indeed, the very capacity to notice and think of refutatory data and ideas was completely gone. Confirmation bias was as if "galloping . . . ," and I could not stop it." (Chadwick, 2007). Chadwick's experience might be cast as a progressive shift from a state of uncertainty populated with odd experiences and ideas without any overarching delusional framework to the strengthening of a few of these beliefs into full-blown delusions whose reliabilities are greatly over-estimated. If early psychosis is associated with a barrage of information that cannot be ignored because the modulation of behaviour and learning by confidence is perturbed, adopting a few beliefs with pathological certainty might be an effective strategy to explain that information away. However, those beliefs are also likely to cause significant distress and functional impairment, such as Chadwick's eventual belief that he had to throw himself under a bus to drive Satan from his body (Chadwick, 1993). As I will expand upon in the final discussion, thinking about the development of nonclinical PEs and clinical psychosis within a

computational framework might allow us to sketch out possible mechanistic pathways by which PEs and psychopathology develop that can be tested in further studies.

This work has a number of strengths. Utilising computational modelling made explicit all the informational quantities and their transformations that could generate task behaviour. It also allowed close comparison with the investigation of Vinckier & colleagues into the computational effects of ketamine. Finally, I utilised a large sample drawn from a representative general population cohort. The study also has limitations. Some data was missing on all variables, but this is offset by use of a large, epidemiologically-principled sample. The task employed is simple and may not be optimal to measure the modulation of behaviour by confidence. While the winning model fit every participant better than chance, there was variation in model fit that could reflect unmeasured computational atypicalities that could be relevant for understanding aberrant mental states. To limit the number of comparisons made, I did not consider possible confounding aetiological factors like cannabis use or IQ. Psychotic phenomena and the task behaviour were not measured at the same time points, with the task data collected around 6 months prior to the time 3 assessments at age 17. The relevance of this task for behaviour in real-world environments is not known but the use of this simple associative task has allowed precise manipulation and modelling of environmental regularities and this provides a basis for extending the framework to more naturalistic observations.

Chapter 12

Anomalous perceptions and beliefs are associated with shifts towards different types of prior knowledge in perceptual inference

Abstract

Psychotic phenomena manifest in healthy and clinical populations as complex patterns of aberrant perceptions (hallucinations) and tenacious, irrational beliefs (delusions). According to predictive processing accounts, hallucinations and delusions arise from atypicalities in the integration of prior knowledge with incoming sensory information. However, the computational details of these atypicalities and their specific phenomenological manifestations are not well characterised. I tested the hypothesis that psychosis-proneness arises from increased reliance on overly-general application of prior knowledge in perceptual inference, generating percepts that readily capture the gist of the environment but inaccurately render its details. I separately probed the use of prior knowledge to perceive the gist versus the details of ambiguous images in a healthy population with varying degrees of hallucination- and delusion-proneness. I found that the use of prior knowledge varied with both the severity of hallucination-proneness and the composition of psychotic phenomena in terms of aberrant percepts versus aberrant beliefs. In contrast to my original predictions, predominant hallucination-proneness conferred an advantage perceiving image details and image gist, consistent with reliance on highly-detailed perceptual knowledge. Predominant delusion-proneness conferred a large disadvantage perceiving image details without disadvantaging perception gist, consistent with reliance on abstract, belief-like knowledge. These findings suggest that phenomenological variability in psychotic experiences may be driven by variability in the type of knowledge observers rely upon to resolve perceptual ambiguity.

12.1 Research Questions

- Are nonclinical psychotic experiences associated with changes in how percepts are generated from ambiguous sensory information using prior knowledge, reflecting over-reliance of prior knowledge?

- Does over-reliance on prior knowledge in perceptual inference make percepts in psychosis-prone people overly-general or inaccurate?
- Is this more associated with proneness to hallucinations and anomalous perceptions, versus proneness to delusions and anomalous beliefs?

12.2 Introduction

Hallucinations and delusions can be modelled within a hierarchical predictive processing framework, in which perceptions and beliefs represent the brain's best inference about the causes of its sensory inputs (Helmholtz, 1860; Lee and Mumford, 2003; Friston, 2005). The general idea of these conceptualisations is that sensation is inherently ambiguous; the brain must combine sensory measurements with prior knowledge of the environment in order to effectively infer what caused those sensations. How much weight is given to sensory evidence and prior knowledge in this combination is determined by their reliabilities (Knill and Pouget, 2004): when sensory information is unreliable, predictions from prior knowledge should be weighted more strongly, and vice versa. The reliabilities of sensory information and prior knowledge also shape learning. When predictions and sensory inputs disagree, this generates 'prediction errors'. Prediction errors might reflect meaningful changes in environmental states, in which case they should be accommodated by learning, i.e., by changing one's predictions through updating internal models. Importantly, however, learning should be scaled to the reliability of information sources, with large changes in internal models taking place only when prediction errors are reliable.

Positive psychotic symptoms may arise when reliability-weighting of information sources goes awry, causing perceptions and beliefs to diverge from objective (Fletcher and Frith, 2009; Adams et al., 2013). Within this framework, hallucinations can be modelled as false inferences, caused by over-weighting the reliability of predictions (Behrendt, 1998; Aleman et al., 2003; Corlett et al., 2009). Delusions may be considered internal models that misrepresent statistical regularities in the environment and could arise through inappropriate learning from unreliable prediction errors (Kapur, 2003). Such models of psychotic phenomena in patients and psychosis-prone people have been tested by manipulating both prior knowledge and sensory input (Schmack et al., 2013; Teufel et al., 2015). In a previous study, in which the authors kept sensory input constant while manipulating prior knowledge, individuals at high-risk of clinical psychosis showed a shift towards greater influence of prior knowledge. This shift was measured as an advantage in discriminating ambiguous images that contained an embedded figure, the perception of which was facilitated by experimentally-provided prior knowledge (Teufel et al., 2015). The advantage was also present in healthy individuals scoring highly on scales of psychosis-proneness. Here, it was particularly related to aberrant perceptions rather than aberrant beliefs.

While this specificity is in line with previous suggestions that hallucinations are a consequence of an increased influence of prior knowledge on perception (Behrendt, 1998; Aleman et al., 2003; Corlett et al., 2009), it provides no further detail about the computational mechanisms bringing about this effect. In the current study, I sought to shed light on the computational principles underlying the psychosis-associated shift towards over-using prior knowledge in perceptual inference. Specifically, I tested the hypothesis that this shift could be computationally explained

by more flexible fitting of predictions to sensory data, causing a strong but imprecise influence of prior knowledge on perception in psychosis-prone observers. This imprecise influence should in turn lead to imprecise, gist-like percepts whenever the perceptual situation demands the use of prior knowledge to resolve ambiguity. I tested this hypothesis with ambiguous images that contained embedded objects, the perception of which required prior knowledge. Holding sensory information constant, I measured how precise observers' percepts of the embedded objects was before and after experimentally providing prior knowledge. I predicted that high hallucination-proneness would be associated with the previously-observed shift towards an undue reliance on prior knowledge but that this would lead to imprecise, gist-like percepts.

12.3 Methods

12.3.1 A model of generating percepts using prior knowledge

To measure the influence of prior knowledge on perception, I investigated observers' perception of figures (humans or other animals) in 'two-tone images', which were generated by binarising natural images around luminance thresholds. Two-tone images were designed to be near-impossible to disambiguate without having prior knowledge of image content. However, by providing prior knowledge through exposure to the natural image from which a two-tone image was generated (labelled the 'template image'), observers are typically readily able to perceive the figure(s) embedded in it (see Figure 12.1b for an example two-tone image).

I model the generation of a coherent percept of such figures as the competitive matching of predictions to sensory evidence (Trapp and Bar, 2015). In this context, the competing predictions are based on memory representations of the template stored as prior knowledge, while sensory evidence is derived from the two-tone image. Subjective percepts might be generated when sufficient sensory information is explained by the winning prediction, analogous to 'accepting' a perceptual hypothesis (Gregory, 1980). Without prior knowledge, the possible hypothesis-space is too large to find a sufficiently well-fitting prediction, thus no figure percept is generated. Prior knowledge of template images greatly narrows this hypothesis-space, for example via semantic image content and sensory properties of illumination and viewpoint (Bar, 2003). More flexible fitting of predictions could be modelled as generating percepts when predictions explain less evidence, so there is greater residual sensory prediction error (Figure 12.1a). In other words, flexible fitting of predictions can be understood as 'accepting' the perceptual hypothesis as adequate on the basis of a weaker fit between hypothesis and data.

Such a change in the cut-off point for what constitutes an acceptable perceptual hypothesis could, under some circumstances, maintain stable percepts even when sensory evidence is unreliable. It could also come with the cost of tolerating greater mismatch between prior knowledge and sensory evidence, predisposing to inaccurate percepts. In extremis, I consider this a model of hallucinations - percepts markedly dissociated from sensory evidence.

Figure 12.1: Schematic of how percepts may be generated from ambiguous two-tone images

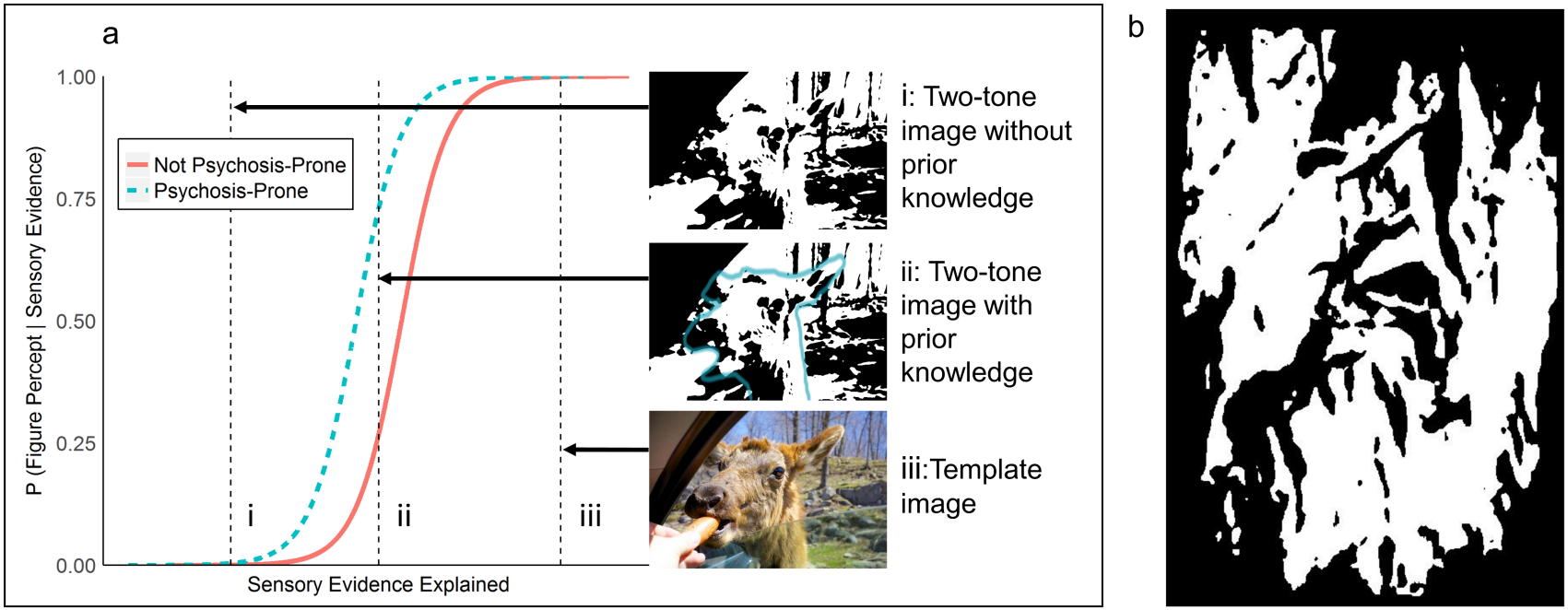


Figure 12.1: a) A simplistic theoretical function that transforms sensory evidence explained by a prediction into the probability of generating a coherent percept of a figure. The amount of sensory evidence that is explained by the prediction is insufficient to produce a meaningful percept when viewing a two-tone image with an embedded figure but with no prior knowledge about it (i). When viewing the non-degraded template image (iii), much of the sensory information is explained and the figure is perceived. When viewing a two-tone image containing an embedded figure with prior knowledge about image content, predictions can be generated that explain more sensory evidence (ii). However, not all evidence is explained due to the loss of visual information in the two-tone image compared to the template. Generating a percept when a lower level of evidence is explained by predictions, which we hypothesis may occur in early psychosis and healthy psychosis-proneness, would result in more figures being generated, but may come at the cost of those percepts misrepresenting the environment, giving rise to anomalous perceptions. b) An example of a two-tone image (see next Figure for corresponding template image).

12.3.2 Task design

In the current study, I designed a task with two conditions using two-tone stimuli. The 'Global' condition was designed such that flexible fitting of predictions to sensory data would confer an advantage and performance would be largely insensitive to the accuracy of the resultant percept. This meant that participants needed only to generate percepts that accurately reflected global image properties, or 'gist', without high levels of detail. The 'Local' condition was designed to penalise inaccurate percepts, meaning participants needed to generate detailed percepts that reflected precise local image properties.

These two conditions were embedded in a novel visual discrimination task in which observers had to make a two-alternative forced choice response as to whether a small red dot, presented somewhere on a two-tone image, was on or off an embedded figure. For each two-tone image in each condition (Global/Local), a pair of dot locations were chosen, one on and one off any embedded figure(s). In the Global condition, paired dot locations were chosen such that they were equidistant from the centre of the image, assuming observers would expect figures to be central. Locations were chosen far from the edges of any figures and, where possible, separated by patches or segments demarcating figure edges, to make the on-figure/off-figure discrimination possible even if generating inaccurate or coarse percepts.

In the Local condition, paired dot locations were chosen equidistant from a figure contour that was present in the template image but invisible in the corresponding two-tone, identified using a fuzzy logic edge-detection algorithm. Dots were placed very close to either side of this invisible contour, so the discrimination required percepts with precise local detail.

Observers made the same set of discriminations before and after gaining prior knowledge by viewing their corresponding template images on 'template trials' ('Pre-Template' and 'Post-Template', respectively). Identical pre-template and post-template trials allowed me to isolate the effects of prior knowledge on perception by examining within-subject change in performance measures after seeing the template image.

12.3.3 Hypotheses

If the stronger influence of prior knowledge that is observed in psychosis is due to a more flexible fitting of predictions to sensory evidence, I would expect that psychosis-proneness, particularly hallucination-proneness, in healthy observers would confer an advantage in the Global condition and disadvantage in the Local condition. This prediction follows because flexible application of prior knowledge would lead to observers generating percepts readily but imprecisely, allowing them to outperform observers who are less likely to generate a percept in the Global condition, in which only gist-like information is necessary to complete the task. In turn, the generation of imprecise percepts should impair performance in the Local condition, in which local information on fine image details is necessary.

12.3.4 Stimuli: Two-tone and Template Images

Stimuli were two-tones (binarised black and white images) and templates (the natural photographs from which two-tones were made, see figures 1b and 2c for an example). To naïve observers who have not seen the corresponding template images, most two-tone images appeared meaningless and were near impossible to disambiguate, even with extended viewing. However, after gaining prior knowledge through viewing the corresponding template image, observers could usually generate percepts of the embedded figure(s). This produces an often striking change in subjective experience, despite identical sensory information. Similar to illusory contours in stimuli such as the Kanizsa triangle (Kanizsa, 1976), observers sometimes even report perceiving the contours of figures in two-tone images, despite those contours not actually being present.

The stimulus set was generated by combining stimuli from Teufel et al. (2015) and novel two-tone stimuli, then piloting and validating images with 4 observers who did not take part in the main experiment. Observers viewed a set of two-tone images, reported what they could see and rated the image for clarity from 1-5, before and after viewing the corresponding template images. 73 suitable images with low clarity ratings before and high clarity ratings after viewing the template images were used as stimuli for the main experiment.

12.3.5 Image Screening

Before the main task, observers were presented with the set of two-tone stimuli and asked to freely report whatever they could see in the image, if anything. In the case that observers thought they could see but not fully recognise a figure, they were encouraged to report where in the image they thought it was. Stimuli in which observers recognised any figure or its approximate location were excluded and the 30 experimental stimuli chosen randomly from the remaining pool.

12.3.6 Trial structure

There were two trial types in this experiment: two-tone trials, in which participants made decisions about dots being on or off figures in two-tone images, and template trials, in which participants acquired prior knowledge about two-tone images by viewing their natural image counterparts (Figure 12.2). Two-tone trials began with a fixation cross on a grey background, then a two-tone image was ramped up in contrast over 200ms. When the two-tone reached full contrast, the dot appeared. After 100ms, the dot flashed off and on for one frame to help observers localise it. The two-tone and dot were presented at full contrast for 700ms then ramped down in contrast over a further 200ms to be replaced with a text prompting observer to respond. Observers had no time limit on making their decision but were instructed to respond as quickly and as accurately as possible.

On each template trial, a two-tone image was first shown for 100ms. Its template image was superimposed and ramped up in contrast over 800ms to give the appearance of smoothly transitioning from two-tone to template. This aided disambiguation and strengthened the subjective percepts of embedded figures. The template image was displayed at maximum contrast for

Figure 12.2: Trial and task structure

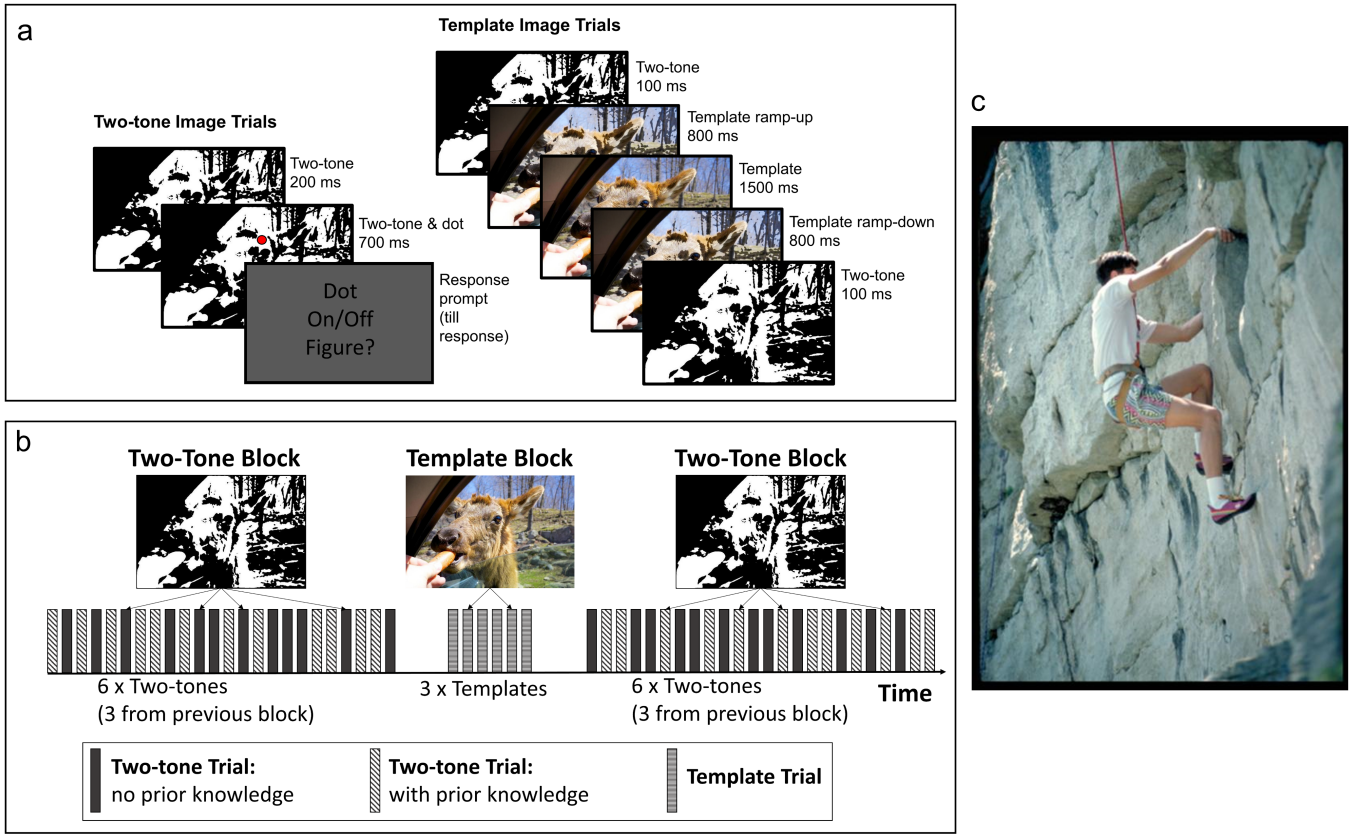


Figure 12.2: a) Observers discriminated whether a dot was on or off a figure embedded in two-tone images in 'two-tone trials'. On each two-tone trial, after a fixation cross, the two-tone image was ramped up smoothly over 200ms, then the dot presented and flashed for one frame to aid localisation. The two-tone and dot were presented for 700ms, then smoothly ramped off to reveal a response prompt. Participants could respond at any time. Observers gained prior knowledge with which to disambiguate two-tone images from template images in 'template trials'. On each template trial, a two-tone was presented for 100ms then its superimposed corresponding template image ramped up smoothly over 800m, so as to blend smoothly from two-tone to template. The template was presented for 1500ms, then ramped down over 800ms to reveal the two-tone for 100ms. b) Trials were grouped into two-tone and template blocks. Each two-tone block contained 24 trials and featured 6 two-tones, each presented 4 times (all combinations of dot on/off, Global/Local condition). Participants had prior knowledge about 3 two-tones in each block; 3 were unfamiliar and participants had no prior knowledge about them. Novel and familiar two-tones were interleaved. Template blocks contained 6 template trials, with 2 repetitions of 3 template images, corresponding to the three unfamiliar two-tones introduced in the previous block. There were 10 two-tone and template blocks in total. c) An example of a template image that corresponds to the two-tone image in Figure 12.1b.

1500ms then ramped down in contrast over 800ms to reveal the two-tone image, which was then ramped down over 100ms.

Stimuli were presented using Matlab (Mathworks) and the Psychophysics Toolbox (Brainard, 1997; Pelli, 1997; Kleiner et al., 2007). Two-tone and template stimuli were 7:5 rectangular and presented on a 15.6" laptop screen with a 60 Hz refresh rate at a distance of approximately 60cm, subtending approximately 17.5° by 12.6°.

12.3.7 Experimental Structure

The experiment was structured into blocks of two-tone trials and template trials (see Figure 12.2b). A two-tone block comprised 6 different two-tone images, each used on 4 trials (two Global trials, one on- and one off-figure; two Local trials, one on- and one off-figure) for a total of 24 trials per block. Prior to every two-tone block, observers were exposed to templates for 3 two-tone images. Thus, pre-template and post-template two-tones were interleaved.

The order of trial types (on-/off-figure) and conditions (Global/Local) was counterbalanced for within-sequence effects and the images randomly sorted into that sequence, with the requirement that the same two-tone image was not shown more than twice in succession. Two-tone blocks alternated with template blocks. In a template block, 3 templates were shown, each on two template trials, for a total of 6 template trials. 30 different two-tone and template images were used in each main experiment, giving 120 two-tone trials before and 120 two-tone trials after template exposure, each with 60 trials in the Global condition and 60 in the Local condition.

12.3.8 Observers

40 healthy individuals (age range (years) = 18-27, mean age = 22.3, SD = 2.14, 25 female) were recruited via online advertisement and student email lists at the University of Cambridge. I required that observers had not previously seen any of the experimental stimuli, had normal or corrected-normal vision, were not colour-blind and had no history of psychiatric or neurological illness. Observers were reimbursed £8 for their time and gave written informed consent after explanation of all experimental procedures and potential consequences. The study was approved by the Cambridge Psychology Research Ethics Committee (Reference PRE.2013.31). I collected all primary data for this study (see Appendix D for participant information sheet and consent form).

12.3.9 Measuring Psychosis-Proneness

I measured two dimensions of proneness to positive psychotic experiences with self-report questionnaires. Delusion-like ideation was measured with the Peters Delusions Inventory (Brief) (Peters et al., 2004), a 21-item questionnaire comprising statements about unusual beliefs. Each item is endorsed as a dichotomous 'yes'/ 'no' answer. Endorsed items are rated on three subscales: 'distress', 'preoccupation' and 'conviction'. The sum score of the subscales was used as the score for each participant. Items that were not endorsed were treated as 0 on the subscales.

Hallucination-like experiences were measured with the Cardiff Anomalous Perceptions Scale (CAPS) (Bell et al., 2006), a 32-item questionnaire comprising a set of statements about unusual perceptual experiences and hallucinations. The format and scoring are the same as for the PDI, though the additional subscales were 'distress', 'frequency' and 'intrusiveness'.

12.3.10 Outcome variables

Perceptual Performance

My primary outcome variable was the observers' ability to discriminate between on-figure and off-figure trials as indexed by *d'*. This index, an objective measure of ability to perform a perceptual discrimination derived from signal detection theory, was calculated for each participant and Dot Condition * Template Exposure combination.

d' was calculated using the following equation:

$$d' = Z(HitRate) - Z(FalseAlarmRate)$$

where Z is the inverse cumulative standard normal distribution function, Hit Rate is the proportion of trials where the dot was correctly identified as on-figure and False Alarm Rate is the proportion of trials where the dot was incorrectly identified as on-figure.

12.3.11 Reaction Times

An increase in *d'* after seeing template images indicates that the observer has access to more evidence relevant to their decision in post- versus pre-template trials. One explanation for such a change might be that higher-quality information is extracted from the two-tone images after template exposure because of the use of prior knowledge to disambiguate the stimuli. Alternatively, observers might take longer to make a decision and thereby accumulate more evidence, which might not necessarily be related to the use of prior knowledge.

To distinguish these possibilities, I conjointly examined reaction times (RTs) and accuracy using a drift-diffusion model (DDM). The DDM is a widely used mathematical model of information processing that represents evidence accumulation on a single trial as a stochastic random-walk process, where a response is emitted when a certain evidence threshold is reached. Access to higher-quality information is modelled as more rapid accumulation of evidence towards a correct decision and parameterised as 'drift rate' (v). Increasing drift rate speeds reaction times and increases accuracy. By contrast, requiring more evidence before making a decision can be parameterised as a change in the 'decision threshol*d'*, the distance between evidence thresholds. Increasing decision threshold increases accuracy but slows reaction times.

A hierarchical DDM was fit to RT data using the 'HDDM' package (Wiecki et al., 2013). In the hierarchical DDM, model parameters for each subject are treated as random effects drawn from group-level distribution (all participants). Hierarchical Bayesian estimation was used to simultaneously estimate group- and subject-level parameters.

I estimated a DDM in which each boundary reflected a decision that the dot was on or off a figure. The parameters of the model were drift rate, decision threshold, non-decision time and a bias parameter, indicating tendency to favour one decision for each observer and condition. The DDM converged appropriately, assessed by Geweke statistics being less than 2, visual inspection of chain posteriors and prediction of reaction time distributions for each subject.

12.3.12 Statistical analyses

First, I tested whether the task conditions and exposure to the template image had the intended effects on *d'*, drift rate and decision threshold by entering values on each outcome into 2x2 factorial ANOVAs with factors Template Exposure (pre-Template / post-Template) and Dot Condition (Global / Local). Follow-up comparisons were performed with paired Welch's t-tests.

I next tested whether the effects of seeing the template on *d'* were attributable to changes in evidence extraction (parameterised by drift rate, v) or in evidence needed to make a decision (parameterised by decision threshold, a). I calculated within-subject change (post-Template – pre-Template) in the Global and Local conditions in *d'*, drift rate and decision threshold ($\Delta d'$, Δv, Δa respectively). I then tested Pearson correlations of $\Delta d'$ with Δv and Δa.

Finally, I tested relationships between dimensions of psychosis-proneness and within-subject change in each outcome variable in the Global and Local conditions, as well as the difference in change between the Global and Local conditions. Therefore, there were three variables per subject for each outcome measure (e.g. for *d'*, these were $\Delta d'_{\text{Global}}$, $\Delta d'_{\text{Detail}}$ and ($\Delta d'_{\text{Global}}$ - $\Delta d'_{\text{Detail}}$).

In order to investigate effects of absolute levels of psychosis-proneness, I entered hallucination-proneness (as estimated by the anomalous perception score) and delusion-proneness (as estimated by the anomalous belief score) into separate univariate regressions predicting each outcome. I next investigated effects of the composition of psychotic phenomena in terms of the balance between anomalous perceptions and anomalous beliefs by entering both hallucination-proneness and delusion-proneness into multivariate regressions predicting each outcome. Therefore, I ran the following regressions for each outcome variable:

$$\Delta y_{condition} = \beta_0 + \beta_1 Hallucination - proneness + \epsilon$$

$$\Delta y_{condition} = \beta_0 + \beta_1 Delusion - proneness + \epsilon$$

$$\Delta y_{condition} = \beta_0 + \beta_1 Hallucination - proneness + \beta_2 Delusion - proneness + \epsilon$$

No interactions between hallucination-proneness and delusion-proneness were considered, due to collinearity. In multivariate regressions, I assessed collinearity by checking that results were constant when predictors were re-ordered and that the variance inflation factor was below 4. Unless otherwise reported, there was no evidence of collinearity.

12.4 Results

2 observers were excluded from the analysis: one for having seen the stimuli in a previous study; another for misunderstanding the instructions, evident upon debriefing.

12.4.1 Psychosis-Proneness

The CAPS and PDI measures showed positive skew that was corrected by square-root transformation (Shapiro-Wilk test, CAPS: $W = 0.96$, $p = 0.25$, PDI: $W = 0.97$, $p = 0.33$). Following transformation, there were no outliers. As expected, hallucination-proneness and delusion-proneness were correlated (Pearson $r = 0.67$, $t = 5.42$, $df = 36$, $p < 0.001$).

12.4.2 Perceptual performance

In the Global condition, 3 observers had a perfect hit rate and 1 participant made no false alarms. To adjust for this and calculate *d'*, hit rates of 1 were replaced with $1 - 1/60$ and the false alarm rate of 0 were replaced with $1/60$ (60 being the number of trials per condition) (Macmillan and Creelman, 2004). Removing these observers from analyses did not change any substantive conclusions.

Figure 12.3: Effects of prior knowledge on perceptual inference

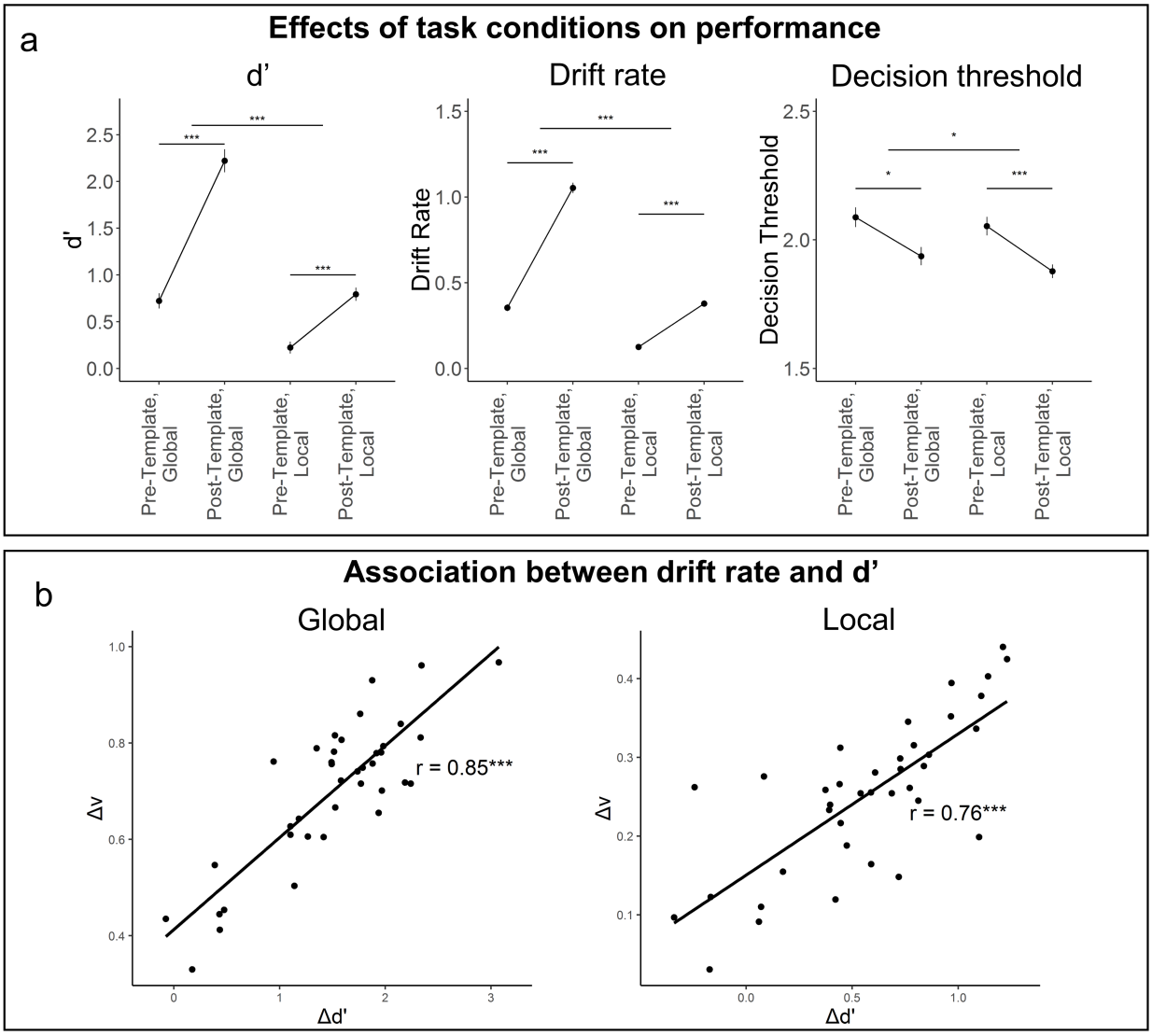


Figure 12.3: a)Effects of task conditions on performance in terms of discriminability index (d', mean ± SEM), rate of evidence accumulation towards a decision (drift rate, from diffusion drift model) and evidence needed to make a decision (decision threshold, from diffusion drift model). Both d' and drift rate increased in both conditions after gaining prior knowledge from template images and increased more in the Global condition than the Local condition. Decision threshold reduced after gaining prior knowledge, indicating that participants required less evidence to make a decision. The reduction was greater for the Local condition than the Global condition. Prior knowledge therefore allowed participants to extract evidence faster and make perceptual decisions based on less evidence. b) Change in d' and drift rate were highly correlated in both the Global and Local conditions, while there were no correlations between change in d' and decision threshold (not shown). This supports that prior knowledge improved performance by enhancing extraction of information from two-tone images.

As expected, prior knowledge facilitated perception of figures embedded in two-tone images (12.3a). This facilitation was indicated by a difference in *d'* between before and after seeing the template (main effect of Template Exposure: $F_{1,\ 40.66}) = 138.64$, $p < 0.001$) and follow-up t-tests, which revealed better performance after having seen the template in both conditions (Global: t = 6.43, df = 37, $p < 0.001$, D = 2.11; Local: t = 8.44, df = 37, $p < 0.001$, D = 2.77). The

Global condition, which required less detailed information, was easier to perform, indicated by an overall main effect of Condition ($F_{1,\ 35.31}$) = 120.39, $p < 0.001$) and higher *d'* in the Global condition than the Local condition both pre- and post-template (Pre-Template: t = 6.43, df = 37, $p < 0.001$, D = 2.11; Post-Template: t = 15.68, df = 37 $p < 0.001$, D = 5.16). Furthermore, the magnitude of improvement was greater in the Global condition than the Local condition, indicated by a Template Exposure * Dot Condition interaction ($F_{1,\ 8.18)}$ = 27.89 $p < 0.001$) and confirmed by follow-up t-test (t = 8.66, df = 37, $p < 0.001$, D = 2.85).

12.4.3 Prior knowledge facilitates perceptual discrimination by improving evidence extraction

Drift diffusion modelling indicated that that prior knowledge facilitated extraction of high-quality evidence from two-tone images rather than observers acquiring more information by waiting longer to respond (12.3a). Drift rate changed as a result of seeing the template, as evidenced by a significant main effect of Template Exposure ($F_{1,\ 148)}$ = 430.5, $p < 0.001$) and was higher after seeing the template than before in both conditions (Global: t = 19.302, df = 37, $p < 0.001$, D = 6.35; Local: t = 20.982, df = 37, $p < 0.001$, D = 6.90).

With respect to a difference between the two conditions, the modelling indicated that evidence was acquired more rapidly about the gist of an embedded figure than about its precise details. Drift rate was different across the Global and Local conditions, indicated by a significant effect of Dot Condition ($F_{1,\ 148)}$ = 477.0, $p < 0.001$) and was higher in the Global condition both before and after template exposure (Pre-Template: t = 11.64, df = 37, $p < 0.001$, D = 3.83; Post-Template: t = 18.29, df = 37, $p < 0.001$, D = 6.02). Importantly, this main effect was qualified by a significant Template Exposure * Dot Condition interaction ($F_{1,\ 148)}$ = 104.8, $p < 0.001$). Together with posthoc tests, which indicated significantly higher increase in drift rate in the Global condition (t = 14.11, df = 37, $p < 0.001$, D = 4.63), this finding suggests that the impact of prior knowledge was stronger for the perception of the gist of a stimulus than its fine details.

In addition to evidence suggesting that prior knowledge facilitated more rapid extraction of evidence from two-tone images, my results suggest that top-down modulation also caused observers to make decisions based on less evidence. This interpretation is suggested by analyses of the decision threshold parameter, which was lower after than before template exposure ($F_{1,\ 148)}$ = 22.490, $p < 0.001$). There were no effects of Dot Condition or interaction effects. Posthoc tests confirmed that decision threshold reduced in both conditions (Global: t = 5.124, df = 37, $p < 0.001$, D = 1.68; Local: t = 7.85, df = 37, $p < 0.001$, D = 2.58).

The prediction that prior knowledge would improve perception of figures embedded in two-tone images mainly by facilitating extraction of information was further supported by a direct comparison between the index of the change in discriminatory performance ($\Delta d'$) due to prior knowledge and model parameter estimates (12.3b). I found a significant Pearson correlation between change in *d'* ($\Delta d'$) in both the Global (r = 0.85, t = 9.56, df = 36, $p < 0.001$) and Local (r = 0.76, t = 57.04, df = 36, $p < 0.001$) conditions with a change in drift rate (Δv) but no relation with change in decision threshold (Δa) (Global condition: r = -0.03, t = -0.21, df = 36, p = 0.83; Local condition: r = -0.12, t = -0.69, df = 36, p = 0.491).

12.4.4 Effects of hallucination-proneness and delusion-proneness on perceptual performance

Univariate analyses of hallucination-proneness and delusion-proneness considered independently

As predicted, and consistent with previous work, hallucination-proneness (total CAPS score) was associated with an advantage in using prior experience to perceive the gist of the figures in two-tone images. This was indicated by association between CAPS and $\Delta d'$ in the Global condition (Figure 4a – dashed line, t = 2.382, p = 0.023, D = 0.79, $r_{equiv.}$ = 0.37) but was not reflected in Δv (Figure 4b – dashed line). Contrary to predictions, hallucination-proneness did not predict a disadvantage in perceiving image details, (though neither did it predict an advantage), shown by lack of relationship with $\Delta d'$ or Δv in the Local condition (Figures 4a & 4b – solid lines). This suggested that hallucination-prone healthy observers' enhanced ability to readily generate template-derived percepts of two-tone images (as evidenced by their advantage in the Global condition) did not come at the cost of an inability to perceive detailed aspects of the images.

There was some (non-significant) evidence that the advantage to perception associated with hallucination-proneness was specific to gist perception, indicated by a trend towards a difference between Δv in the Global and Local conditions (t = 1.853, p = 0.072, D = 0.62, $r_{equiv.}$ = 0.3). This effect was not apparent in $\Delta d'$.

In contrast to hallucination-proneness, I found no relationship between delusion-proneness (total PDI score) and experience-dependent perception of the gist of figures, indicated by an absence of association with $\Delta d'$ or Δv in the Global condition (Figures 4c & 4d – dashed lines). This suggested that the advantage in generating percepts of figures, based upon experience of the templates, could be specific to anomalous perceptions, rather than anomalous beliefs. Interestingly, I found evidence that the predicted psychosis-associated disadvantage in perceiving image details was associated with delusional ideation. In the Local condition, delusion-proneness (total PDI score) predicted smaller Δv (Figure 4d – solid line, t = -2.278, p = 0.029, D = 0.76, $r_{equiv.}$ = -0.35) and trend-predicted smaller $\Delta d'$ (Figure 4c – solid line, t = -1.83, p = 0.076, D = -0.61, $r_{equiv.}$ = -0.29). Higher PDI scores also predicted larger differences in discrimination of image gist and details, indicated by difference in $\Delta d'$ across conditions (t = 2.32, p = 0.026, $r_{equiv.}$ = 0.36, D = 0.77).

Multivariate analyses of hallucination-proneness and delusion-proneness considered together

My prediction of hallucinations-associated advantage in perceiving the gist of embedded figures was therefore borne out by the data but I found only weak evidence of a disadvantage in perceiving image detail. This was associated with proneness to delusions (PDI scores), rather than hallucinations (CAPS scores). However, I observed striking and opposing effects of hallucination- and delusion-proneness when the balance between these dimensions of positive psychotic phenomena was considered by entering both into multivariate linear regressions. Being excessively

Figure 12.4: Trial and task structure

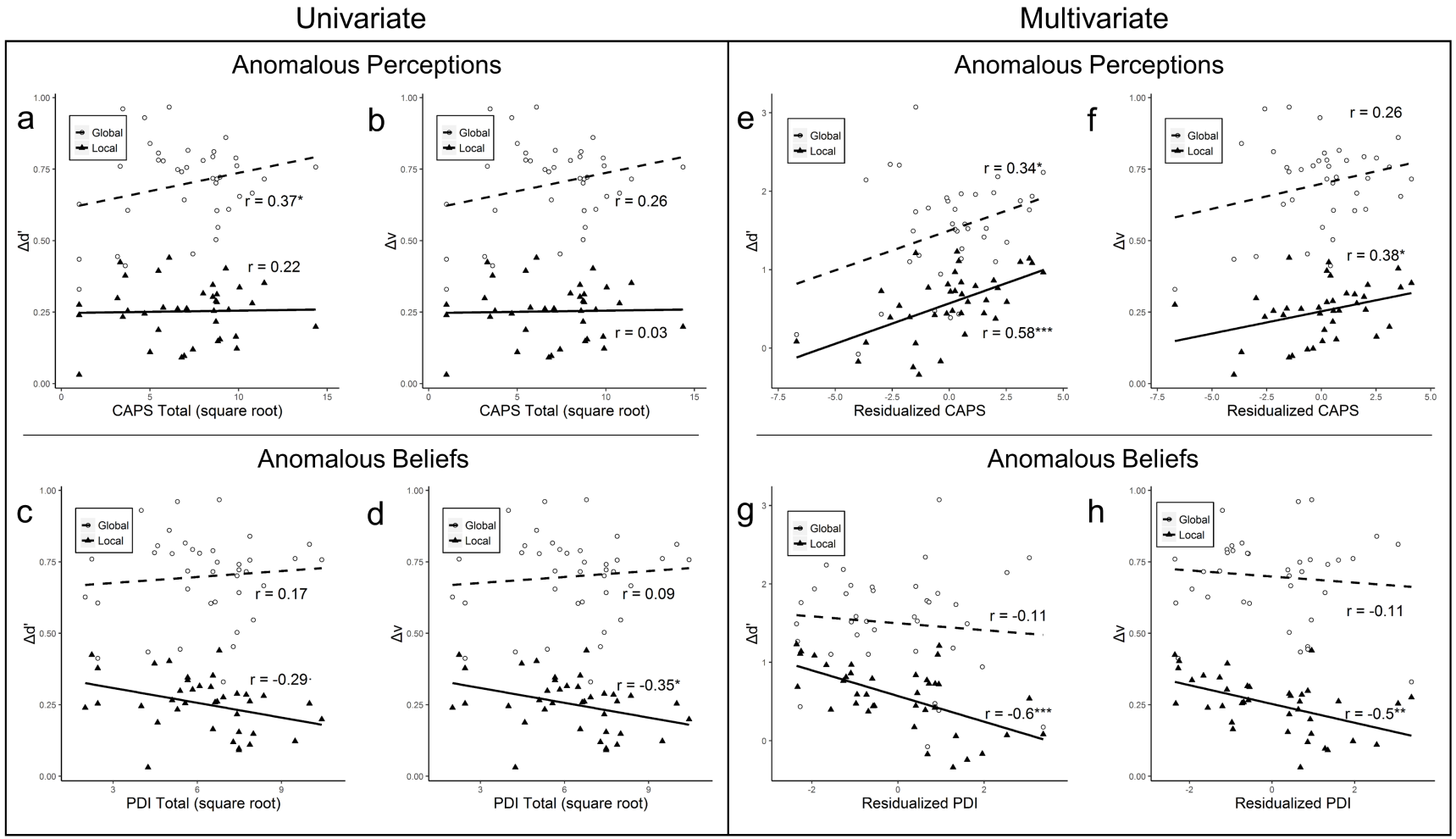


Figure 12.4: Univariate regressions showed an association between hallucination-proneness and greater improvement in discriminability ($\Delta d'$) with template exposure (Figure 12.4a) but this was not reflected in change in drift rate (Δv) (Figure 12.4b). Delusion-proneness trend-predicted lower $\Delta d'$ and predicted lower Δv in the Local condition (Figure 12.4c & 12.4d). Multivariate regressions showed a different pattern of results. Predominance of hallucination-proneness predicted greater $\Delta d'$ in the Global condition (Figure 4e) but also greater $\Delta d'$ and Δv in the Local condition (Figures 4e and 4h). In contrast, predominance of delusion-proneness predicted lower $\Delta d'$ and Δv in the Local condition (Figures 12.4g & 12.4h). Reported r-values are equivalent correlations estimated from linear regressions.

or predominantly hallucination-prone, for a given level of delusion-proneness, conferred moderate advantage using prior knowledge to perceive image gist, shown by greater $\Delta d'$ in the Global condition (Figure 4e – dashed line, t = 2.17, p = 0.037, D = 0.72, $r_{equiv.}$ = 0.34), further associating greater readiness to generate percepts with hallucination-like experiences. However, this association was not reflected in Δv (Figure 4f – dashed line, t = 1.61, p = 0.117, D = 0.54, $r_{equiv.}$ = 0.26).

Importantly, predominant hallucination-proneness also predicted a large advantage using prior knowledge to perceive image details, shown by greater $\Delta d'$ and Δv in the Local condition ($\Delta d'$: Figure 4e – solid line, t = 4.23, p < 0.001, D = 1.41, $r_{equiv.}$ = 0.58; Δv : Figure 4f – solid line, t = 2.43 p = 0.02, D = 0.81, $r_{equiv.}$ = 0.38), reflecting generation of detailed percepts that were highly faithful to the template information. This advantage was not strongly specific to one condition, shown by absence of an association with difference in $\Delta d'$ or Δv across the Global and Local conditions. Observers who were more strongly prone to anomalous perceptions than delusional ideation therefore more readily generated percepts of figures embedded in two-tone images with a high degree of accurate image detail.

In contrast, being predominantly delusion-prone, for a given level of hallucination-proneness, did not predict an advantage or disadvantage in perceiving gist, but the details were perceived aberrantly with respect to the optimal template-derived percepts. This was indicated by an absence of a relationship between predominant delusion-proneness and $\Delta d'$ or Δv in the Global condition (Figures 4g & 4h – dashed lines), but a large disadvantage in the Local condition ($\Delta d'$: Figure 4g – solid line, t = -4.48, p < 0.001, D = -1.51, $r_{equiv.}$ = -0.60, Δv : Figure 4h – solid line, t = -3.43, p = 0.002, D = -1.14, $r_{equiv.}$ = -0.5). There was weak evidence that delusion-predominance conferred different effects on discrimination of gist and details, shown by a trend towards greater difference in $\Delta d'$ across the conditions (t = 1.72, p = 0.093, D = 0.57, $r_{equiv.}$ = 0.28), though this was not evident in drift rate. Observers who were more strongly prone to delusional ideation than anomalous perceptions were therefore able to generate percepts of embedded figures, but their perception of those figures' details differed from the information provided by the template images.

Critically, there were no associations between change in decision threshold with Template exposure and either hallucination-proneness or delusion-proneness, in univariate or multivariate regressions. This supports an assertion that the observed changes in perceptual performance, indexed by *d'*, were unlikely to be caused by a change in the amount of evidence needed to make decisions, which might have reflected strategy more than a change in the extraction of information from visual percepts.

12.5 Discussion

In the current study, I sought to understand psychosis-proneness more fully by exploring mechanisms of the integration of sensory evidence with prior knowledge across different levels of hallucination and delusion-proneness. Specifically, I used ambiguous images containing embedded figures, the perception of which was aided by prior knowledge, to test the hypothesis that hallucination-proneness is related to a tendency to generate percepts despite a poor fit between

actual sensation and predictions derived from prior knowledge. According to this hypothesis, hallucination-proneness should be related to better extraction of image gist in perceptual situations that heavily rely on prior knowledge, but an impairment in extracting fine image detail.

Though partly borne out, my results demand a more complex explanation. First, in keeping with my prediction and with previous results (Teufel et al., 2015) I showed that hallucination-proneness was associated with a greater ability to use prior knowledge to generate percepts, which is consistent with the idea that anomalous perceptions arise from a changed integration of sensory evidence with top-down predictions (Corlett et al., 2009, 2010; Fletcher and Frith, 2009). However, hallucination-proneness did not predict inaccurate perception of image details. Indeed, when I considered within-individual balance between hallucination- and delusion-proneness, I found that higher levels of aberrant perception in the context of lower levels of aberrant beliefs was associated with better perception of both image gist and fine details. Critically, diffusion-drift modelling showed that this improvement was not due to strategy differences as might have been indicated by changes in decision threshold but was driven by more efficient visual extraction of evidence. While supporting the idea that hallucinations arise from over-reliance on top-down predictions, this shows that, contrary to my expectations, prior knowledge supports visual extraction of highly-detailed perceptual information in hallucination-prone observers who lack anomalous beliefs. Conversely, observers with higher levels of aberrant belief in the context of lower levels of aberrant perception were relatively disadvantaged when using prior knowledge to perceive local details of embedded figures. This disadvantage was driven by less efficient evidence extraction, rather than changing decision thresholds. However, predominantly delusion-prone observers showed intact perception of image gist. Thus delusion-proneness specifically was associated with using prior knowledge to visually extract information pertaining to the images' broad meanings but poorly extracting information about their precise details.

I suggest that these findings, though complex, may actually be explicable by considering a processing hierarchy ascending from concrete, unimodal sensory inputs to more abstract, belief-like levels (Mumford, 1992; Friston et al., 2006). Within this framework, the advantage held by hallucination-prone and the disadvantage befalling delusion-prone observers could both be conceived of in terms of a computational shift towards over-reliance on prior knowledge in perceptual inference. Critically, the different performance capabilities of delusion-prone and hallucination-prone observers could arise from shifts towards relying on prior knowledge originating from different levels of the processing hierarchy.

Predominantly hallucination-prone observers might largely encode and use prior knowledge gained from the template images as perceptual information, conferring an advantage in the task condition that specifically probed knowledge of precise perceptual details. While advantageous in the context of the current experiment, under natural viewing conditions this may result in a tendency to interpret ambiguous sensory information using perceptual hypotheses, predisposing to aberrant generation of percepts and, in extremis, hallucinations.

Conversely, predominantly delusion-prone observers might largely encode template prior knowledge as more abstract, belief like information at high hierarchical levels. Template knowledge encoded or used at these levels would have sufficient information to broadly infer the coarse gist of two-tone images but be of limited use when inferring specific details, as low-level features of

the template would be summarised at the higher level without being specifically encoded. The details of resultant percepts may therefore be volatile or subtly inaccurate. This would explain preserved performance in the gist condition and poor performance in the detail condition. I suggest two possible manifestations of this computational shift in natural viewing conditions. Firstly, observers may tend to interpret ambiguous sensory information by invoking higher-level beliefs, manifesting bizarre or delusional appraisals of events. Secondly, observers may be insensitive to fine perceptual details, particularly when they are not consistent with high-level beliefs. Percepts would effectively be sculpted to conform to expectations, which could manifest as false inferences e.g. wrongly inferring intentions of others from subtle facial expressions.

Central to the account presented here is that psychotic phenomena are associated with unreliability in signalling of low-level sensory information in the visual system. Support for this can be found in the large body of evidence showing dysfunction of early visual processing in psychotic disorders (for review, see Javitt, 2009) and a smaller body of evidence showing similar visual impairments associated with schizotypal personality (for review, see Ettinger et al., 2015). These deficits in early stages of processing may result in the outputs of early processing being noisier and less well-structured, causing ambiguity in perceptual inference and prompting adaptive reliance on top-down predictions from prior knowledge.

These findings provide a starting point for understanding the considerable heterogeneity of positive psychotic phenomena, a heterogeneity that is observed both in clinical samples and the general population but that is poorly addressed by current theoretical models. Isolated anomalous perceptions or beliefs may represent compensatory changes in use of prior knowledge at a single locus of a processing hierarchy, e.g., aberrant use of perceptual or abstract knowledge. Concurrence of both phenomena may occur when adaptation at a single level is not sufficient to resolve unreliability in sensory inputs and the early outputs of sensory processing, leading to a propagation of atypicalities in the use of prior knowledge throughout the processing hierarchy. Indeed, epidemiological evidence suggests that psychotic phenomena may become clinically relevant as anomalous perceptions are complicated by anomalous beliefs (Smeets et al., 2012). Using a nonclinical sample limited my ability to generalise these findings to psychotic disorders, though I can make readily testable predictions about the computational mechanisms of clinical psychotic symptoms. Mapping out computational changes and their neurobiological implementations in early psychosis in relation to changes in health and functional outcomes may therefore allow better prediction of risk based on underlying mechanisms and could suggest new targets and timeframes for pharmacological or psychological intervention.

There is a potential paradox here: while my findings seem to suggest a psychosis-associated advantage in perceptual organisation, there are well-established findings of deficits in perceptual organisation in schizophrenia (for review, see Silverstein & Keane, 2011), and some evidence of abnormal perceptual organisation in schizotypy (Uhlhaas and Silverstein, 2005). These studies tended to find failure in Gestalt perception of stimuli similar to two-tone images, like Mooney faces, and the favouring of local details over global percepts, in contrast with my findings. Psychotic disorders and schizotypy are also associated with deficits, rather than advantages, using predictions in visual perception (Schmack et al., 2015), eye movements (Spering et al., 2013) and predicting consequences of self-made actions (Shergill et al., 2005; Teufel et al., 2010). While this may seem to contradict my findings, the pattern of psychosis-associated predictive

and organisational deficits in the literature is consistent with noisy, overly-influential sensory information, which is at the core of my interpretation of my findings. I suggest that organisational and predictive deficits arise when higher-level knowledge is not available and predictions must be generated 'endogenously'. Noise in the early stages of processing may cause difficulty in selecting or accessing appropriate prior knowledge, but the provision of hypotheses that explain sensory input, as is the case with the template images here, allows reliance on those hypotheses, translating into a task advantage.

To conclude, my results shed light on the emergence and persistence of two seemingly very different atypical experiences, anomalous perceptions and anomalous beliefs, with transdiagnostic relevance for emerging mental disorders. These phenomena may arise from a common computational mechanism, the over-reliance on prior knowledge in the generation of percepts, expressed at different levels of the information processing hierarchy.

Chapter 13

General Discussion

In this thesis, I investigated PEs in young people in the general population in terms of their measurement, association with distress and health implications, their relationship to the social environment and their mechanisms in terms of atypical information-processing. Below, I discuss the overall implications of these studies and make recommendations for future investigations.

13.1 The measurement of psychotic experiences

Further investigation is required into the measurement properties of PEs by different instruments, with the aim of rigorous comparison of instruments and synthesis of different approaches to the study of psychosis, namely the high-risk and schizotypy fields. My results are promising for the integration of work in these different frameworks in that a self-report instrument of current 'schizotypal' phenomena measured the same factor as an interview for discrete lifetime PEs that may be more comparable to clinical instruments. However, there are likely to be significant limitations with even widely-used instruments, making more thorough validation necessary. I found significant problems with the Schizotypal Personality Questionnaire (Raine, 1991) that were largely overcome through re-specification of its dimensional structure. The assessment pathway laid out in Chapter 6 is a reasonable and tractable set of analyses that provide far more information than standard psychometric validation procedures, which are often limited to reporting Cronbach's coefficient alpha or test-retest reliability. This pathway could be standardised and applied to other instruments, so as to obtain more directly comparable information about different instruments measuring PEs. In particular, a critical advance in measurement of PEs would be better understanding of what severity ranges of PEs are measured by different instruments. As in Chapter 5, this might allow us to infer whether 'false-positive' PEs detected by self-report instruments but not verified by interview instruments are actually reflecting PEs at a lower level of severity than an interview is able to measure. The pathway I used is far from exhaustive, and other measures can provide complementary information, depending on the goals of psychometric analysis, such as equipercentile-linking for instruments that should be very directly comparable (Kolen and Brennan, 2006; Fusar-Poli et al., 2016).

An important advance for the field, and for psychiatry and cognitive neuroscience, would be more readily rejecting the use of instruments that show inadequate measurement precision or, at least,

down-weighting the contributions made to the field by studies that use them. Doing so would require direct comparison of multiple instruments but may enable standardisation across different conceptual approaches (schizotypy, high-risk, broader investigations into psychiatry) and a concerted effort to modulate the impact of studies where conclusions are strongly confounded by measurement error. This process might be aided by the construction of standardized validation procedures and extensive simulation of how measurement precision affects the conclusions of empirical research.

13.2 The health implications of psychotic experiences

Psychotic experiences are heterogeneously associated with distress but some PEs index transdiagnostic risk of mental disorders. The results of latent variable modelling and latent class clustering in Appendix C and Chapter 7 support that some but not all PEs are associated with psychopathology, consistent with evidence from the schizotypy field (Mohr and Claridge, 2015), from investigations into selected samples of adults (Brett et al., 2007; Sommer et al., 2010; Peters et al., 2016) and population-based cohort studies (Kaymaz et al., 2012; Kelleher et al., 2012b; van Nierop et al., 2012; Zammit et al., 2013). Between 4.5% and 10% of young people were prone to PEs alongside depressive symptoms, anxious symptoms, social anxiety, poor wellbeing and greatly increased risk of non-psychotic mental disorders. This suggests some PEs commonly occur in young people who are severely distressed (Stochl et al., 2015) and is consistent with comorbidity of PEs in common non-psychotic mental disorders (Kelleher et al., 2012b; Wigman et al., 2012; Fusar-Poli et al., 2014a), evidence that PEs become more likely with increasing severity of non-psychotic psychopathology (Guloksuz et al., 2015) and evidence that psychotic and non-psychotic psychopathologies share environmental (Wigman et al., 2012; van Nierop et al., 2015; Guloksuz et al., 2016) and genetic risk factors (Cross-Disorder Group of the Psychiatric Genomics Consortium et al., 2013; Jones et al., 2016; Zavos et al., 2016).

In contrast, between 7.5% and 15.3% of young people were prone to PEs, including those occurring persistently for over a year, but had low levels of depressive and anxious symptoms and high perceived wellbeing. Arguably, I found little evidence of a completely 'benign' psychosis-prone phenotype, in that the non-distressed, PE-prone cluster in each sample were more likely to have symptoms in other domains or meet criteria or be help-seeking for non-psychotic disorders than young people with neither PEs nor distress. Nonetheless, those young people had far more favourable current mental health than those with PEs and distress and are likely to have far more favourable future health trajectories, though longitudinal work is necessary to confirm this.

Clearly, PEs have heterogeneous health implications, ranging from being relatively benign to indicating either high levels of sub-clinical psychopathology or full-blown mental illness. The specific nature of the PEs young people are prone to and other features, like their social functioning or environmental risk factors, may determine health outcomes.

Different types of PEs appeared to be differently associated with psychopathology and need for clinical care, with paranoid ideation and delusions being more maladaptive than non-paranoid unusual perceptions and beliefs. This is consistent with evidence that clinical psychosis may

develop as delusions and maladaptive appraisals complicate unusual perceptions (Ford, 1995; Smeets et al., 2012a, 2012b, 2015) and that some perceptual PEs and 'magical thinking' can occur relatively benignly (Sommer et al., 2010; Tabak et al., 2013; Brett et al., 2014; Daalman et al., 2016; Peters et al., 2016). I found that young people prone to PEs and distress were more likely to have high levels of paranoia, while those with PEs and low distress had low levels of paranoia. Similarly, paranoid ideation, but not unusual perceptions and beliefs, predicted higher distress one year later in Chapter 8.

Other factors predicted and might cause different health outcomes in young people to PEs. In particular, I found strong evidence for the involvement of a person's early and recent social environment in predicting and possibly shaping health outcomes in people with PEs.

13.3 The social environment may be critical in determining psychotic experiences and psychopathology

A person's social environment may be critical for predicting and/or determining the occurrence and health impact of PEs. Focusing on childhood adversity and recent social support, I found evidence that particular features of social relationships during different developmental periods have different effects on dimensions of PEs and psychopathology in later life.

Childhood adversity predisposed to non-paranoid PEs, paranoid ideation and depressive symptoms and was associated with PEs occurring both with and without high levels of distress. This is consistent with existing literature linking PEs to clinical psychosis (Varese et al., 2012) and to nonclinical PEs (Lovatt et al., 2010; Daalman et al., 2012). I discussed a number of proposed mechanisms by which early life adversity may predispose to PEs in computational terms by appealing to the predictive processing framework and tested one such mechanism directly in an experimental study, though found no evidence that childhood adversity predisposes to PEs by perturbing the modulation of behaviour by confidence.

The quality of recent relationships and social support from family and friends showed different patterns of association with PEs and psychopathology, when compared to childhood adversity. Recent social support clearly separated the distressed and non-distressed PE-prone phenotypes. In longitudinal studies in both the NSPN and ROOTS cohorts, supportive recent relationships reduced depressive symptoms and paranoid ideation but had less effect on non-paranoid unusual perceptions and beliefs. Furthermore, over one year, asocial dispositions promoted PEs and distress, mediated by impairment of social support, suggesting social difficulties are temporally precedent to increases in PEs. Given that childhood adversity was associated with both PE-prone phenotypes, this raises the possibility that adversity in early life may induce shifts in information-processing that tend towards PEs, but that the more recent social environment shapes their content and the implications they have on mental health. This adds to existing work showing that decline in social functioning precedes the onset of psychosis (Velthorst et al., 2016) and that atypicalities in social functioning are present in young people who go on to develop adult schizophrenia (Jones et al., 1994; Malmberg et al., 1998). The recent social environment may therefore be a critical feature in determining health trajectories and, importantly, may represent an under-utilised intervention target to promote positive mental health.

A key remaining question is whether impairments to social functioning and social relationships are symptomatic of the same disease processes that cause PEs or are actually a causal factor in their aetiology, such as through the mechanisms I elaborated on in computational terms. The former would still support their use as predictors, but the latter would suggest they may be valuable therapeutic targets. It is also possible that social deficits may be somewhere between symptomatic and causal. Impairments to social functioning or impoverishment of social relationships may generate a positive feedback cycle, where valuable socially-derived information is lost and the stress-buffering effects of social support are diminished, leading to the acceleration of psychopathology and destabilisation of reality. Causality cannot be inferred from my work alone, but interventions targeting quality of social relationships and networks have shown promising early results (McFarlane et al., 2003; O'Brien et al., 2014; Poulton et al., 2014; Harrop et al., 2015). In future work, it will be important to directly test the proposed mechanisms and map out the pathways by which the social environment influences PEs and psychopathology in terms of information-processing and its neurobiological implementation.

13.4 The mechanisms of psychotic experiences

13.4.1 PEs in adolescents and a pharmacological model of psychosis share a common computational association: a reduction in the modulation of learning by confidence

Current models based on predictive processing posit that the central computational atypicality in psychosis is a perturbation to how the brain signals the reliability of information sources, whether predictions from internal models or incoming evidence collected via the senses. I investigated whether this might be mathematically modelled as a reduction in how people use confidence in their knowledge of the world to modulate their behaviour in an experimental task in a large sample of adolescents. I found that young people did modulate their behaviour according to a parameter that represented confidence and that non-paranoid anomalous experiences and beliefs were associated with a set of changes in information-processing, including reduced modulation of learning by confidence. This is very similar to the findings of a recent study showing that ketamine, a pharmacological model of psychosis, impairs the use of confidence to modulate behaviour in healthy volunteers. These findings therefore support that PEs are associated with atypicalities in how the reliability of internal models shapes learning, and suggest investigation of atypicalities in NDMA receptor function as a potential neurobiological implementation.

13.4.2 The specific content of psychotic experiences may arise from the influence of different types of prior knowledge on perceptual inference

The heterogeneity of PEs in terms of aberrant perceptions and aberrant beliefs might be explained by a common mechanism of aberrant integration of prior knowledge and incoming information, with different manifestations depending on what form in which prior knowledge is encoded. PEs are associated with a greater influence of prior knowledge on perception of ambiguous images (Teufel et al., 2015). I tested a theory that was conceptually similar to the theory elaborated

earlier that adversity and PEs were associated with adaptations to information-processing to mitigate unreliable information about the environment. I hypothesised that PEs, and anomalous perceptions in particular, would be associated with tendency to generate percepts in perceptual inference from a lower level of match between predictions from internal models and actual sensory evidence, as a result of the outputs of early stages of visual processing being less well-structured and less reliable. This would tend towards stabilising perception despite unreliable information, but may come at the cost of generating gist-like or inappropriate percepts, lacking in accurate details and misrepresenting the world. In extremis, this might generate hallucinations and overtly anomalous perceptions.

While I found evidence that increasing proneness to anomalous perceptions predicted greater reliance on prior knowledge to perceive the gist of ambiguous images, I found that the balance between PEs manifesting as anomalous perceptions and beliefs had distinct patterns of association with use of prior knowledge to perceive image detail. Predominance of anomalous perceptions, over anomalous beliefs, predicted far greater ability to perceive details of ambiguous images, driven by more efficient visual extraction of information. This would be consistent with preferential encoding and/or use of prior knowledge as a perceptual code in perceptual inference. In ecological conditions, this may result in inappropriate use of perceptual knowledge to explain ambiguous sensory information, generating false or aberrant percepts.

In contrast, predominance of anomalous beliefs over anomalous perceptions was associated with far worse ability to perceive details of ambiguous images, driven by less efficient visual extraction of information. This would be consistent with preferential encoding/use of prior of prior knowledge in a more abstract, belief-like code that allowed perception of coarse image gist but contained only overly-general or volatile information about image details. This might be a mechanism by which delusion-prone people are largely able to navigate the world but may experience it subtly differently, shaped to conform to expectations and beliefs. This could tend towards delusional appraisals of experiences and also to the persistence of aberrant beliefs by failing to learn from contradictory information.

These results represent early evidence of how probing information-processing using principles and methods from computational neuroscience may further our understanding of behaviours or subjective experiences. In particular, these results provide a starting point to understand the considerable heterogeneity of the content of PEs in mechanistic terms.

13.5 Future directions

13.5.1 Utilising heterogeneity: Mapping computational pathways to psychosis and psychopathology

Heterogeneity has been a recurrent theme in this thesis, and the considerable diversity of PEs and the people who experience them, even within single categories, like those meeting criteria for high psychosis-risk, have been highlighted in recent reviews (Murray and Jones, 2012; Fusar-Poli et al., 2014c; Yung and Lin, 2016). Heterogeneity in pathophysiological mechanisms underlying PEs and mental illness is almost certainly not reflected by current psychiatric nosol-

ogy, despite their reliability and considerable utility. Understanding this heterogeneity might enable psychiatry to move towards 'precision-medicine' (Disease, 2011; Insel, 2014), predicting and tailoring interventions based on underlying disease mechanisms. The hope is that this would enable primary prevention of mental illnesses, maximise intervention efficacy and see the end of time-consuming trial-and-error approaches to therapeutic choices that can leave disease processes running unhindered for long periods.

In future work, it will be critical to take a broad perspective on the development of PEs and psychopathology, considering diverse trajectories towards good and poor health outcomes and psychotic and non-psychotic disorders. From these and other results, I have sketched out crude mechanistic pathways to different health outcomes in young people prone to PEs (Figure 13.1) that could form the basis of further investigations. I do not claim that this model offers much in terms of unique insights into psychosis or its various health outcomes; it fairly closely resembles Meehl's ground-breaking conceptualisation of schizotypy (Meehl, 1962, 1990). Rather, it is an attempt to link epidemiological observations to potential computational mechanisms. I have attempted to take a developmental perspective, so the model shows how PEs might develop across time from a common starting point and three branch-points determining progression towards different health outcomes in people prone to PEs. At the branch points, arrows show that genetic and environmental influences may be critical in determining trajectories.

Perturbations to the signalling of reliability of information is at the core of this model and the earliest atypicality (13.1, A). The results of this perturbation may be that the system is exposed to an excess of information without a well-tuned signal of its reliability. I would suggest that this stage is likely to span childhood or early adolescence and may be associated with transient anomalies in perception and experience but likely without great distress or functional impairment. Due to the complex computations involved in social behaviour, more extreme perturbations might manifest as subtle social abnormalities (Jones et al., 1994).

The first branch-point in the model (13.1, 1) describes whether the perturbation to reliability signalling might subside on its own (B), perhaps through normal development or removal of some driving influence, or whether it drives changes to information-processing (C). If the former, then PEs are likely to subside without negative consequences for health or functioning. In the latter case, exposure to excessive unreliable information may lead to updates to internal models as an attempt to incorporate the new information, tending towards forming beliefs that diverge from the social consensus. It may also drive compensatory over-weighting of some predictions from internal models as an attempt to ignore or explain-away the incoming signals, a consequence of which might be false inferences and aberrant perceptions (Aleman et al., 2003; Teufel et al., 2015).

The second branch-point (13.1, 2) describes whether the early compensatory changes tend towards adjustments that are maladaptive and harmful (D) or adaptive and less harmful (E). Maladaptive adjustments might include developing beliefs that explain unreliable information but are themselves distressing or impairing, such as persecutory beliefs or negative beliefs about the self or the world. These might confer risk of developing mental disorders, particularly non-psychotic disorders like depression, anxiety or substance dependence. I suggest that individuals meeting criteria for high-risk for psychosis would be at this stage of the pathway, as would at least some of the young people belonging to the 'distressed and PE-prone' clusters in the NSPN

Figure 13.1: Linking epidemiological evidence to computational mechanisms

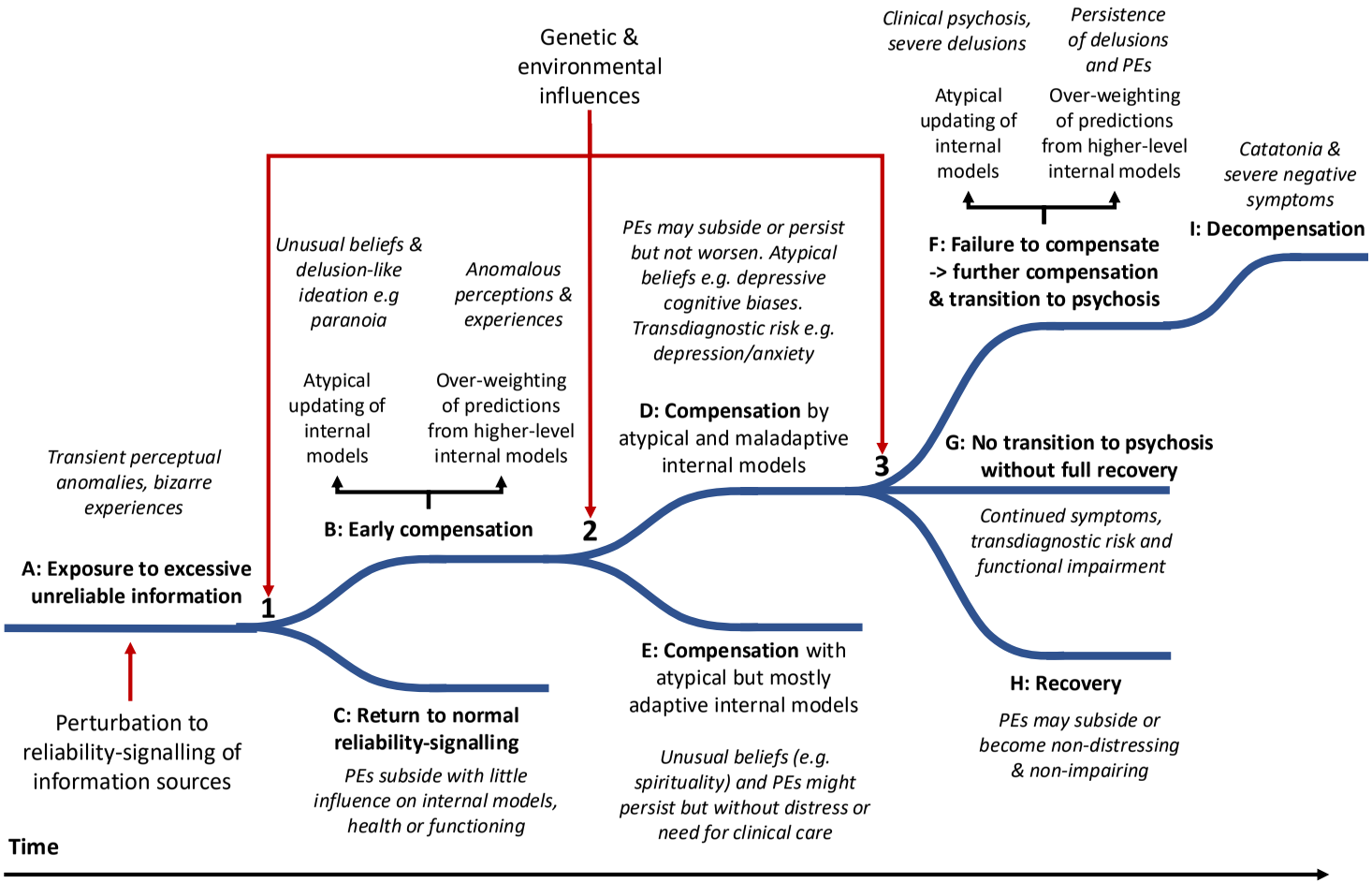


Figure 13.1: This figure outlines a model of the computational mechanisms by which different health outcomes develop in young people prone to psychotic experiences.

and ROOTS cohorts.

Adaptive adjustments might include developing beliefs that explain unreliable information but are not distressing, such as spiritual appraisals (Farias et al., 2013; Brett et al., 2014). The compensation described here need not be at the 'macro-scale' of someone developing explanations for why they had a hallucination, but could instead describe small adjustments to internal models and their reliability-weighting with subtle manifestations in behaviour and personality. With adaptive adjustments, unreliable information might be compensated for and depending on how internal models and their reliabilities were updated, PEs might subside or persist without distress or impairment. I suggest that people manifesting persistent PEs without need for care (Peters et al., 2016), 'healthy schizotypy' (Tabak et al., 2013) and some of the young people belonging to the 'non-distressed, PE-prone' phenotype in NSPN and ROOTS would be at this stage of the pathway.

What factors might determine trajectories from this branch-point? The updating of internal models might depend critically on the information present in the environment. The results of clustering analyses and longitudinal modelling in this thesis suggest that a supportive social environment might be a key determining feature, via various mechanisms discussed previously (though I cannot infer causality from my findings). Causality is supported by early evidence that interventions targeting family and peer relationships are beneficial in clinical psychosis (McFarlane et al., 2003; O'Brien et al., 2014; Poulton et al., 2014; Harrop et al., 2015) but it remains to be seen whether improving social support at a far earlier stage in the development of psychopathology might be a protective and preventative factor for mental disorders.

The third branch-point describes health trajectories in people who have already made maladaptive adjustments to internal models and their reliabilities. Assuming this state corresponds to people at high-risk for psychosis, we can estimate that roughly one third of people will transition to psychosis (Kaymaz et al., 2012), one third will recover fully and one third will continue to have symptoms and functional impairment without transition to psychosis (Schlosser et al., 2012; Simon et al., 2013).

In those who transition to psychosis (path F), I suggest that compensatory changes at stage D will have failed to explain away unreliable information, perhaps because of more severe perturbation to reliability-signalling. The result might be a more dramatic shift in internal models such that they greatly diverge from social consensus and their predictions are ever-increasingly relied upon. The result might effectively be a switch from a state of pervasive uncertainty to pathological certainty in a few aberrant beliefs that cannot be challenged or disproven: Chadwick's 'galloping confirmation bias (Chadwick, 2007), as discussed in Chapter 9. If even these extreme adjustments fail to resolve unreliable prediction error, the result might be an eventual exhaustion of the brain's capacity to adjust. I tentatively suggest that this 'decompensation' might manifest as extreme negative symptoms and catatonia, as the system comes to experience the environment as essentially impossible to predict and all functions that might depend on predictions, like perception and movement (Friston et al., 2010), are fundamentally impaired.

For those who do not transition to psychosis but have continued symptoms and impairment (path F), the system may have managed to mostly stabilise itself in the face of unreliable prediction error, preventing catastrophic distortion of reality, but at a significant cost. The brain's internal

models might now represent the world as a distressing or threatening place and impair things like social interaction as well as confer general risk of mental disorders. However, some will make a full recovery (path H), suggesting they have managed to resolve unreliable prediction error signals but without maintaining maladaptive internal models. Again, the trajectories at branch-point 3 are likely to be influenced by various genetic and environmental factors, like access to clinical interventions or a supportive social environment.

It is important to note what this model does not capture. It neglects negative symptoms and reduces the development of highly complex disorders like depression into a few general statements. It may also be that people at any one stage of the model who are indistinguishable by symptom or computational phenotypes are fully separable at other levels of explanation, such as neurobiological implementation or environmental exposures. It may also be that some individuals are committed to a certain outcome from very early on, such as from a risk factor with a large effect size like 22q11.2 deletion syndrome, so their pathway may feature fewer or different branch-points. Branch-points and a plurality of health outcomes might be an artefact of mixing populations with similar phenotypes but totally different computational or neurobiological mechanisms or aetiologies. People who have made adaptive adjustments to account for unreliable prediction error signalling might still develop maladaptive adjustments and psychopathology, particularly if exposed to environmental risk factors. The 'stages' and 'branch-points' are obviously simplifications; adaptive versus maladaptive adaptation is likely to form a distribution rather than divide into two distinct groups.

Future work might focus on mapping out these pathways in greater detail and testing the computational changes responsible for development of different phenotypes. Critically, studies should seek further evidence of atypicalities in reliability-signalling of information and its association with PEs in the general population, ideally seeking convergent evidence from computational modelling of behaviour and brain function. Beyond this, there may be different sets of environmental risk/protective factors for each branch-point, some of which might be suitable intervention targets. Understanding computational phenotypes for each stage might also allow targeted interventions, such as working to promote adaptive appraisals at branch-point 2 but also working to undo maladaptive adjustments and re-learn healthy models of the world at branch-point 3. Understanding neurobiological implementations at each stage might allow for precision medicine and principled selection of pharmacological or psychological therapy. Longitudinal work in both general population and clinical samples of young people at high-risk for psychosis and mixed-disorder samples will be critical for identifying putative intervention targets and mechanistically-distinct subgroups, which might then form the basis of randomised trials to test causality/clinical effectiveness.

13.5.2 Computational methods offer precision, rigour and explanatory power to bridge the gaps between brain and behaviour

I argue that advances in understanding of psychosis and psychopathology would be facilitated by adopting computational approaches to psychiatry, which equip us with powerful techniques to investigate heterogeneity (Huys et al., 2016), act as a bridge between physical and mental states (Montague et al., 2012; Corlett and Fletcher, 2014; Friston et al., 2014) and encourage

a higher standard of theoretical and methodological rigour (Teufel and Fletcher, 2016). That said, computational methods and frameworks are not without their drawbacks, often appearing opaque to general audiences and being overly flexible, to the point of not being useful (Teufel and Fletcher, 2016). Computational psychiatry is an emerging field and will have to address these issues. Computational approaches might best be considered an adjunct to, rather than a replacement of existing fields, acting as a common language to translate between psychological and neurobiological theories of mental illness.

Computational approaches might be at their most powerful when integrated with epidemiological principles of investigation and inference. The study in Chapter 11 is an example of how a study on information-processing mechanisms can be strengthened by using epidemiologically-principled sampling and utilising longstanding epidemiological frameworks to guide inferences of causality. Identifying whether a computational change is the causal mechanism underlying an association is complicated by the gaps in current understanding of how physical states generate mental states. Some of these problems can be overcome by well-designed interventions. Firstly, mental states may be underpinned by multiple independent sets of computations, so computational changes may not be necessary nor sufficient to produce behavioural changes. Testing this requires high-powered studies that investigate heterogeneity of mechanisms and can identify subgroups of people with similar behavioural phenotypes but distinct computational phenotypes. Secondly, the computational mechanisms by which a person develops and recovers from an atypical mental state may be independent. Testing this requires longitudinal studies that investigate the computational changes accompanying development and recovery from mental disorders. Finally, the same computations may have different physical implementations. Similar to the first point, testing this requires investigations that utilise, rather than ignore, heterogeneity in neurobiology.

13.5.3 Looking beyond positive psychotic phenomena

If our aim is to understand clinical psychosis and its development, my results also support more recent shifts in opinion that it is time to look beyond 'positive' psychotic phenomena to other domains like negative symptoms, affective symptoms and social impairments, and indeed to more holistic investigations of mental health in young people, rather than 'siloed' thinking about specific disorders (Fusar-Poli et al., 2014b). Bebbington (2015) argues that current conceptualisations of psychosis, with positive symptoms at the core and other symptoms, like mood disturbance and social and cognitive impairments as 'ancillary' symptoms, are inadequate because the core of psychotic symptoms is poorly-defined and non-specific (Bebbington, 2015). This is likely to be particularly true when looking not at established disorder but at subclinical expression of apparently disorder-like phenomena, such as PEs in the general population.

However, given that psychotic phenomena manifest in clustering patterns that cut across traditional diagnostic boundaries and are comorbid in non-psychotic disorders, it may be appropriate to investigate them in the context of broader, transdiagnostic approaches to the early manifestations of mental illness, such as empirical staging models based on disease severity (McGorry et al., 2014). Such approaches could be clinically useful and could enable unbiased investigation and refinement of disorder constructs based on unfolding disease processes. For example, the

model sketched out in 13.1 might represent a way to establish stages based on both symptom and computational phenotypes, but even that is likely to be too focused on PEs. This endeavour would be aided by better characterisation of the computational and neurobiological pathophysiology that underlie symptoms and syndromes across disorders and symptom domains and how they are influenced by genetic and environmental factors.

13.6 Conclusion

Psychotic experiences are some of the most puzzling and fascinating phenomena studied in clinical neuroscience. Furthering our understanding of psychotic phenomena might shed light on the development of disorders that impose a heavy burden of suffering on individuals and their loved ones and great demands on health services, but might also help us answer fundamental questions about how our subjective experience of the world is generated from physical states in the body and why it differs from person to person. In this thesis, I attempted to comprehensively investigate psychotic experiences in young people in the general population, from their measurement to their health implications and computational mechanisms. My work suggests that, while there are issues with their measurement, different conceptual approaches to studying psychotic experiences might well be synthesised with the hope of seeding collaboration and conversation across different lines of enquiry. Psychotic experiences in young people, while not entirely benign, are heterogeneously associated with psychopathology. Importantly, they characterise a minority of the general population who are at very high transdiagnostic risk of mental illness. Health outcomes in young people with psychotic experiences are predicted and potentially modified by the social environment, signifying potential for novel strategies for risk stratification and intervention. Psychotic experiences and even their phenomenological manifestation as anomalous perceptions versus anomalous beliefs might be understandable in computational terms as disruptions to the signalling of reliability of information and consequent adaptations. The application of computational approaches to psychiatry might yield greater understanding of the mechanisms and aetiology of psychotic phenomena and, indeed, all psychiatric disorders by bridging the explanatory gap between physical and mental states. In doing so, we might revolutionise the way that we conceptualise, identify and manage mental illness for the better of those who experience it.

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Appendices

Appendix A

The neurobiological implementation of typical and atypical predictive processing

A.1 The neurobiological implementation of predictive processing

Predictive coding could be plausibly implemented by neurobiological circuits (Rao and Ballard, 1999). Predictive processing only requires representing a few informational quantities and their 'intrinsic' connections within each level of processing and their 'extrinsic' connections to other levels of processing. The architecture at each level can be repeated in layers above and below. In this way, it may be possible to describe a 'canonical microcircuit' as a general unit of neuronal organisation that could serve as the basic unit of computations (Douglas et al., 1989; Douglas and Martin, 1991). The canonical microcircuit would need to represent bottom-up sensory evidence/prediction error, either from sensory detectors or unexplained information from the level below. It would need to represent descending predictions of incoming inputs, derived from stored internal models. It would need to represent lateral connections within each level that guide selection of predictions. It would also need to represent the precision of each signal (Bastos et al., 2012).

Regarding algorithms, it would need to compare the prediction with the sensory evidence and compute a prediction error within a level and, based on their precision, update the predictions it makes of lower levels and pass prediction error upwards to the higher level with a certain precision (Friston, 2010).

Recent work has mapped these quantities and algorithms onto the activity of certain neuronal populations and their connections (Bastos et al., 2012). The neocortex has a columnar structure (Mountcastle, 1997) with 6 layers and is considered hierarchically arranged (Felleman and Van Essen, n.d.). The architecture of connections in a cortical column is well-suited to implement predictive coding (Mumford, 1992; Rao and Ballard, 1999; Haeusler and Maass, 2007), potentially forming a canonical microcircuit.

Ascending prediction error may be signalled by excitatory superficial pyramidal cells in layers 2-3 (L2/3), also called 'supragranular' layers because they are above the granular layer (L4) (Bastos et al., 2012). Descending predictions may be conveyed by excitatory deep pyramidal cells in layer 5 (L5), also called 'infragranular' layers because they are below L4 (Bastos et al., 2012). Predictions of inputs could be conveyed by deep pyramidal cells that project to superficial cortical layers at the level below (Felleman and Van Essen, n.d.). These projections may be conveyed to interneurons rather than pyramidal cells directly. These connections might be driven primarily by glutamatergic signalling via NDMA receptors (Self et al., 2012).

L4 serves as the input layer for ascending prediction error, receiving projections from L2-3 at the level below, possibly primarily driven by glutamatergic signalling via AMPA receptors (Self et al., 2012). From L4, prediction

errors could be conveyed by intrinsic connections to the superficial pyramidal cells at that level. In those superficial cortical layers, excitatory and inhibitory interneurons convey predictions from deep cortical layers and enable comparison of predictions and inputs to generate prediction errors (Bastos et al., 2012).

Prediction errors could then be conveyed by intrinsic connections to deep pyramidal cells in layer 5 (L5), allowing the changing of predictions. L5 pyramidal cells could then pass new predictions both to L4 at the same level by intrinsic connections, allowing iterative attempts to minimise prediction error (Bastos et al., 2012). L5 pyramidal cells could also project to superficial layers at the level below, via extrinsic feedback connections (Felleman and Van Essen, n.d.), attempting to explain incoming evidence at the lower level with updated predictions.

The structural properties of cortical layers, such as their relative thicknesses, change across brain areas but patterns of intrinsic and extrinsic connectivity remain similar (Weiler et al., 2008; Lefort et al., 2009), though specific proportions of feedforward & feedback connections change (Barone et al., 2000), perhaps reflecting tuning to specific information types and precisions of informational quantities. The dynamics of these properties suggest that different spectral properties of neuronal firing, such as power in specific frequency bands, should be asymmetrical in superficial and deep cortical layers (Wang, 2010). Specifically, prediction errors should be conveyed by high-frequency gamma-band neural oscillations. Predictions should be conveyed by lower-frequency (alpha/beta-band) oscillations. Recent principled investigations support these spectral asymmetries (Bosman et al., 2012; Bastos et al., 2015; Michalareas et al., 2016). Advances in neuroimaging have enabled investigation of layer-specific neural signalling in humans that support predictive coding (Petro et al., 2014; Muckli et al., 2015; Morgan et al., 2016).

Precision-weighting may be conveyed by slower neuromodulators or neuronal synchrony. In particular, tonic dopamine firing is thought to convey the precision of prediction errors (Friston et al., 2009), which determines the extent of model updating that they drive. This is consistent with evidence that tonic dopamine firing encodes uncertainty or violation of expectations (Fiorillo et al., 2003; Preuschoff et al., 2006). This is in contrast to the phasic firing of dopamine that signals reward prediction error (Montague et al., 1996; Schultz et al., 1997). Precision-weighting may also rely on intact functioning of excitation and inhibition within the canonical microcircuit: in particular, the modulation of synchronisation and of synaptic gain by inhibitory GABAergic interneurons and the forwards and backwards message-passing driven by excitatory AMPA and NMDA glutamatergic signalling (Bastos et al., 2012).

A.2 Mapping abnormalities in information-processing on to neurobiological implementation

How well does disrupted predictive processing explain the atypical neurobiology associated with clinical psychosis and nonclinical PEs? I briefly cover four major neurobiological alterations implicated in schizophrenia: abnormalities in the neurotransmitters dopamine, glutamate and GABA, and disrupted neural connectivity.

A.2.1 Dopamine

Schizophrenia is associated with increased presynaptic dopaminergic signalling, with increase in dopamine synthesis capacity, baseline synaptic dopamine and dopamine release, evident on brain imaging (Howes et al., 2012), supported by post-mortem studies (Owen et al., 1978; Mackay et al., 1982; Kaalund et al., 2014) and genetic associations (Schizophrenia Working Group of the Psychiatric Genomics Consortium et al., 2014). Successful antipsychotic medications all antagonise D2 dopamine receptors (though also affect other dopamine receptors and other neuromodulator systems). Meta-analysis supports a small but heterogeneous effect of increased D2/3 receptor availability in schizophrenia (Howes et al., 2012), which may be an upregulation in response to anti-dopaminergic medication (Howes et al., 2015). In people at high-risk for psychosis, there is evidence of increased dopamine synthesis capacity (Howes et al., 2009, 2011; Mizrahi et al., 2012) but also studies reporting no difference (Bloemen et al., 2013; Suridjan et al., 2013). In otherwise healthy people with auditory PEs, the only study to date has shown no increase in dopamine synthesis capacity (Howes et al., 2013). Increased presynaptic dopamine may be a state marker of clinically relevant psychotic symptoms. This would fit with the proposed computational

role of dopamine as signalling the precision of prediction errors, implemented by modulating synaptic gain on superficial pyramidal cells. Inappropriate release of dopamine may therefore result in over-weighting the precision of prediction errors and inappropriate attribution of salience (Winton-Brown et al., 2014), causing aberrant inference and model updating. However, it is not known why nonclinical PEs would not be associated with increased presynaptic dopamine. Nonclinical PEs may have different neurobiological implementation, but further studies are necessary to establish this.

A.2.2 Glutamate

Evidence supports dysfunction of NDMA glutamate receptors in schizophrenia from post-mortem studies (Humphries et al., 1996; Sokolov, 1998), in-vivo imaging (Marsman et al., 2013; Poels et al., 2014) and genetic loci associated with the disease (Schizophrenia Working Group of the Psychiatric Genomics Consortium et al., 2014). Results in high-risk groups are inconclusive (Howes et al., 2015). Further suggestion of NMDA dysfunction comes from the use of NMDA receptor antagonists, like ketamine and phencyclidine (PCP), which induce psychotic symptoms and psychosis-like cognitive disturbances (Krystal et al., 1994; Javitt, 2007). NMDA receptor dysfunction may impair passing of top-down predictions from internal models to be compared with sensory inputs (Corlett et al., 2007), perturbing the computation and use of prediction errors. Specifically, NMDA dysfunction might result in sensory activity that is not explained away by predictions, leading to a pervasive sense of uncertainty and inappropriate learning of associations from aberrant prediction errors (Corlett et al., 2009). A recent study tested the computational effects of ketamine administration on reinforcement learning in healthy volunteers. Ketamine disrupted the influence of a parameter akin to confidence (that increased with correct choices and decreased with incorrect choices) on learning and behaviour, supporting that ketamine may induce uncertainty by reducing capitalisation on learned contingencies (Vinckier et al., 2016), which could predispose to aberrant learning of associations.

A.2.3 GABA

GABA is the major inhibitory neurotransmitter in the brain, expressed mainly in interneurons that regulate spike timing, neuronal oscillatory rhythms and synchronisation, playing a critical role in regulating the behaviour of neuronal circuits (Möhler, 2007). Dysfunction in GABAergic signalling and interneuron function are implicated in schizophrenia (Lewis et al., 2005; Nakazawa et al., 2012; Gonzalez-Burgos et al., 2015) and may explain neurophysiological abnormalities like reductions in gamma-band oscillations (Uhlhaas and Singer, 2010). In high-risk groups, one study has shown increased levels of GABA in the striatum and medial prefrontal cortex (de la Fuente-Sandoval et al., 2016), while another showed reduced binding potential of striatal GABA receptors (Kang et al., 2014). Given the ubiquity of GABAergic signalling, the precise computational implications of GABAergic dysfunction are not well-known, though alterations in GABA signalling are associated with abnormalities in surround-suppression in early visual processing in schizophrenia (Yoon et al., 2010).

A.2.4 Dysconnectivity

The 'disconnection hypothesis' of schizophrenia posits that the key pathology is in modulation of neuronal plasticity and causes impairments in communication across distributed neuronal populations (Friston, 1998). Advances in network science and methods like connectomics have enabled the mapping of structural and functional brain connectivity with unprecedented detail. Schizophrenia is associated with deficits in short-range and long-range neural synchronisation (Uhlhaas and Singer, 2010) and abnormal organisation of brain networks (van den Heuvel and Fornito, 2014). One study has examined structural brain networks in psychosis high-risk groups and found similar changes in network organisation as those observed in schizophrenia (Schmidt et al., 2016). Dysconnectivity might arise as a result of abnormal maturation processes (Uhlhaas and Singer, 2011), such as consolidation of brain network hubs that occurs in adolescence and is influenced by expression of schizophrenia risk genes (Whitaker et al., 2016). Dysconnectivity is likely to be a complex phenotype that arises from distributed molecular or cellular pathology, such as the abnormalities in the neuromodulator systems discussed above. Mapping

whole brain networks on to specific computations is immensely challenging and the influences of dysconnectivity on information-processing are not well-understood.

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Appendix B

Parameter estimates from latent variable models

B.1 Parameter estimates of models from Chapter 4

Table B.1: Pooled parameter estimates from Raine's (1991) 9-factor SPQ model, fit to 25 imputed datasets with a robust weighted-least-squares (WLSMV) estimator. Unstd. estimate ūnstandardised estimate. Std. estimate s̄tandardised estimate.

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	IOR	1	1	0	NA	NA	0.35
Loading	IOR	10	1.67	0.15	11.39	<0.001	0.58
Loading	IOR	19	2.11	0.18	11.75	<0.001	0.74
Loading	IOR	28	1.78	0.15	11.77	<0.001	0.62
Loading	IOR	37	1.77	0.15	11.63	<0.001	0.62
Loading	IOR	45	2.02	0.17	11.69	<0.001	0.71
Loading	IOR	53	2.24	0.19	11.9	<0.001	0.78
Loading	IOR	60	2.38	0.2	11.88	<0.001	0.83
Loading	IOR	63	2.37	0.2	11.96	<0.001	0.83
Loading	SA	2	1	0	NA	NA	0.77
Loading	SA	11	1.06	0.03	30.26	<0.001	0.81
Loading	SA	20	0.71	0.04	18.92	<0.001	0.54
Loading	SA	29	1.03	0.03	31.02	<0.001	0.79
Loading	SA	38	1.09	0.03	31.78	<0.001	0.84
Loading	SA	46	1.21	0.03	36.14	<0.001	0.93
Loading	SA	54	0.57	0.04	13.94	<0.001	0.44
Loading	SA	71	1.19	0.03	34.92	<0.001	0.91

Table B.1 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	MT	3	1	0	NA	NA	0.68
Loading	MT	12	1.04	0.07	15.42	<0.001	0.71
Loading	MT	21	1.11	0.08	14.62	<0.001	0.76
Loading	MT	30	0.96	0.06	15.05	<0.001	0.65
Loading	MT	39	1.07	0.08	13.11	<0.001	0.73
Loading	MT	47	1.09	0.07	15.5	<0.001	0.74
Loading	MT	55	1.14	0.08	14.54	<0.001	0.77
Loading	UPE	4	1	0	NA	NA	0.63
Loading	UPE	13	0.99	0.05	20.58	<0.001	0.62
Loading	UPE	22	1.01	0.07	14.27	<0.001	0.63
Loading	UPE	31	1.04	0.05	19.69	<0.001	0.65
Loading	UPE	40	1.16	0.06	17.95	<0.001	0.73
Loading	UPE	48	1.21	0.06	18.76	<0.001	0.76
Loading	UPE	56	0.94	0.05	17.18	<0.001	0.59
Loading	UPE	61	1.22	0.05	23.51	<0.001	0.77
Loading	UPE	64	1.22	0.05	22.96	<0.001	0.77
Loading	OB	5	1	0	NA	NA	0.83
Loading	OB	14	0.92	0.03	32.93	<0.001	0.77
Loading	OB	23	1.07	0.02	44.06	<0.001	0.9
Loading	OB	32	1.04	0.03	40.37	<0.001	0.87
Loading	OB	67	1.11	0.03	44.38	<0.001	0.93
Loading	OB	70	0.93	0.03	35.98	<0.001	0.78
Loading	OB	74	0.92	0.04	22.16	<0.001	0.77
Loading	NCF	6	1	0	NA	NA	0.59
Loading	NCF	15	1.31	0.07	18.64	<0.001	0.77
Loading	NCF	24	1.25	0.07	18.47	<0.001	0.73
Loading	NCF	33	1.3	0.07	18.48	<0.001	0.76
Loading	NCF	41	1.22	0.07	17.4	<0.001	0.71
Loading	NCF	49	0.73	0.06	12.74	<0.001	0.43
Loading	NCF	57	1.33	0.07	18.97	<0.001	0.78
Loading	NCF	62	0.97	0.07	14.25	<0.001	0.57
Loading	NCF	66	1.41	0.07	18.87	<0.001	0.83
Loading	OS	7	1	0	NA	NA	0.73
Loading	OS	16	0.79	0.04	20.36	<0.001	0.58
Loading	OS	25	0.82	0.04	20.81	<0.001	0.6
Loading	OS	34	0.8	0.04	20.61	<0.001	0.59
Loading	OS	42	1.05	0.04	25.94	<0.001	0.77

Table B.1 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	OS	50	0.92	0.04	24.18	<0.001	0.67
Loading	OS	58	0.96	0.04	24.95	<0.001	0.7
Loading	OS	69	1.11	0.04	30.13	<0.001	0.81
Loading	OS	72	1	0.04	25.53	<0.001	0.73
Loading	CA	8	1	0	NA	NA	0.75
Loading	CA	17	0.97	0.03	29.34	<0.001	0.73
Loading	CA	26	1.01	0.05	22.19	<0.001	0.76
Loading	CA	35	0.92	0.04	23.63	<0.001	0.69
Loading	CA	43	1.01	0.04	28.87	<0.001	0.76
Loading	CA	51	0.91	0.04	25.44	<0.001	0.68
Loading	CA	68	0.81	0.04	22.53	<0.001	0.6
Loading	CA	73	0.97	0.03	28.23	<0.001	0.73
Loading	SUS	9	1	0	NA	NA	0.76
Loading	SUS	27	0.84	0.03	27.13	<0.001	0.64
Loading	SUS	36	1.09	0.03	34.32	<0.001	0.84
Loading	SUS	44	0.93	0.03	29.58	<0.001	0.71
Loading	SUS	52	0.98	0.03	30.23	<0.001	0.75
Loading	SUS	59	1.06	0.03	31.23	<0.001	0.81
Loading	SUS	65	0.9	0.03	27.9	<0.001	0.69
Intercept	0 -> 1	1	0.24	0.03	9.31	<0.001	0.24
Intercept	0 -> 1	10	0.18	0.03	7.13	<0.001	0.18
Intercept	0 -> 1	19	0.6	0.03	21.83	<0.001	0.6
Intercept	0 -> 1	28	0.81	0.03	27.94	<0.001	0.81
Intercept	0 -> 1	37	1.17	0.03	35.24	<0.001	1.17
Intercept	0 -> 1	45	0.4	0.03	15.03	<0.001	0.4
Intercept	0 -> 1	53	0.37	0.03	14.01	<0.001	0.37
Intercept	0 -> 1	60	0.39	0.03	14.7	<0.001	0.39
Intercept	0 -> 1	63	0.16	0.03	6.2	<0.001	0.16
Intercept	0 -> 1	2	0.39	0.03	14.68	<0.001	0.39
Intercept	0 -> 1	11	0.56	0.03	20.5	<0.001	0.56
Intercept	0 -> 1	20	-0.06	0.03	-2.45	0.01	-0.06
Intercept	0 -> 1	29	-0.2	0.03	-7.87	<0.001	-0.2
Intercept	0 -> 1	38	-0.33	0.03	-12.6	<0.001	-0.33
Intercept	0 -> 1	46	0.27	0.03	10.45	<0.001	0.27
Intercept	0 -> 1	54	-0.55	0.03	-20.31	<0.001	-0.55
Intercept	0 -> 1	71	0.32	0.03	12.12	<0.001	0.32
Intercept	0 -> 1	3	1.12	0.03	34.37	<0.001	1.12

Table B.1 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Intercept	0 -> 1	12	1.11	0.03	34.17	<0.001	1.11
Intercept	0 -> 1	21	0.77	0.03	26.89	<0.001	0.77
Intercept	0 -> 1	30	1.02	0.03	32.52	<0.001	1.02
Intercept	0 -> 1	39	1.5	0.04	37.85	<0.001	1.5
Intercept	0 -> 1	47	1.33	0.04	36.97	<0.001	1.33
Intercept	0 -> 1	55	1.45	0.04	37.76	<0.001	1.45
Intercept	0 -> 1	4	0.15	0.03	5.73	<0.001	0.15
Intercept	0 -> 1	13	0.51	0.03	18.9	<0.001	0.51
Intercept	0 -> 1	22	1.49	0.04	37.86	<0.001	1.49
Intercept	0 -> 1	31	0.99	0.03	32.16	<0.001	0.99
Intercept	0 -> 1	40	1.39	0.04	37.33	<0.001	1.39
Intercept	0 -> 1	48	1.37	0.04	37.22	<0.001	1.37
Intercept	0 -> 1	56	0.79	0.03	27.33	<0.001	0.79
Intercept	0 -> 1	61	0.49	0.03	18.39	<0.001	0.49
Intercept	0 -> 1	64	0.66	0.03	23.67	<0.001	0.66
Intercept	0 -> 1	5	0.28	0.03	10.68	<0.001	0.28
Intercept	0 -> 1	14	0.47	0.03	17.45	<0.001	0.47
Intercept	0 -> 1	23	0.05	0.03	1.94	0.015	0.05
Intercept	0 -> 1	32	0.8	0.03	27.53	<0.001	0.8
Intercept	0 -> 1	67	0.6	0.03	21.82	<0.001	0.6
Intercept	0 -> 1	70	0.43	0.03	16.17	<0.001	0.43
Intercept	0 -> 1	74	1.36	0.04	37.22	<0.001	1.36
Intercept	0 -> 1	6	1.05	0.03	33.13	<0.001	1.05
Intercept	0 -> 1	15	0.12	0.03	4.77	<0.001	0.12
Intercept	0 -> 1	24	0.51	0.03	19.03	<0.001	0.51
Intercept	0 -> 1	33	0.46	0.03	17.08	<0.001	0.46
Intercept	0 -> 1	41	0.83	0.03	28.33	<0.001	0.83
Intercept	0 -> 1	49	0.43	0.03	16.28	<0.001	0.43
Intercept	0 -> 1	57	0.33	0.03	12.42	<0.001	0.33
Intercept	0 -> 1	62	1.35	0.04	37.09	<0.001	1.35
Intercept	0 -> 1	66	0.76	0.03	26.66	<0.001	0.76
Intercept	0 -> 1	7	0.45	0.03	16.73	<0.001	0.45
Intercept	0 -> 1	16	-0.12	0.03	-4.82	<0.001	-0.12
Intercept	0 -> 1	25	-0.27	0.03	-10.22	<0.001	-0.27
Intercept	0 -> 1	34	0.08	0.03	3.09	<0.001	0.08
Intercept	0 -> 1	42	0.91	0.03	30.23	<0.001	0.91
Intercept	0 -> 1	50	0.34	0.03	13.09	<0.001	0.34

Table B.1 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Intercept	0 -> 1	58	0.18	0.03	7.04	<0.001	0.18
Intercept	0 -> 1	69	0.66	0.03	23.84	<0.001	0.66
Intercept	0 -> 1	72	0.9	0.03	30.2	<0.001	0.9
Intercept	0 -> 1	8	0.53	0.03	19.64	<0.001	0.53
Intercept	0 -> 1	17	0.15	0.03	5.81	<0.001	0.15
Intercept	0 -> 1	26	1.5	0.04	37.79	<0.001	1.5
Intercept	0 -> 1	35	1.12	0.03	34.37	<0.001	1.12
Intercept	0 -> 1	43	0.98	0.03	31.9	<0.001	0.98
Intercept	0 -> 1	51	0.7	0.03	24.93	<0.001	0.7
Intercept	0 -> 1	68	0.85	0.03	28.96	<0.001	0.85
Intercept	0 -> 1	73	-0.23	0.03	-9.03	<0.001	-0.23
Intercept	0 -> 1	9	0.25	0.03	9.77	<0.001	0.25
Intercept	0 -> 1	27	-0.05	0.03	-2.12	0.013	-0.05
Intercept	0 -> 1	36	0.62	0.03	22.51	<0.001	0.62
Intercept	0 -> 1	44	0.56	0.03	20.52	<0.001	0.56
Intercept	0 -> 1	52	-0.03	0.03	-1.01	0.031	-0.03
Intercept	0 -> 1	59	1.03	0.03	32.89	<0.001	1.03
Intercept	0 -> 1	65	0.57	0.03	20.99	<0.001	0.57
Residual		1	0.88	0	774.55	<0.001	0.88
Residual		10	0.66	0	337.8	<0.001	0.66
Residual		19	0.46	0	148.23	<0.001	0.46
Residual		28	0.61	0	229.61	<0.001	0.61
Residual		37	0.62	0	156.29	<0.001	0.62
Residual		45	0.5	0	142.4	<0.001	0.5
Residual		53	0.39	0	150.21	<0.001	0.39
Residual		60	0.3	0	142.3	<0.001	0.3
Residual		63	0.31	0	108.17	<0.001	0.31
Residual		2	0.41	0	184.83	<0.001	0.41
Residual		11	0.34	0	115.16	<0.001	0.34
Residual		20	0.7	0	323.87	<0.001	0.7
Residual		29	0.37	0	137.81	<0.001	0.37
Residual		38	0.29	0	122.23	<0.001	0.29
Residual		46	0.14	0	55.22	<0.001	0.14
Residual		54	0.81	0	420.38	<0.001	0.81
Residual		71	0.16	0	62.82	<0.001	0.16
Residual		3	0.54	0	115.47	<0.001	0.54
Residual		12	0.5	0.01	93.21	<0.001	0.5

Table B.1 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Residual		21	0.43	0	113.66	<0.001	0.43
Residual		30	0.57	0	118.65	<0.001	0.57
Residual		39	0.47	0.01	66.36	<0.001	0.47
Residual		47	0.45	0	120.45	<0.001	0.45
Residual		55	0.4	0.01	68.39	<0.001	0.4
Residual		4	0.61	0	248.88	<0.001	0.61
Residual		13	0.61	0	262.15	<0.001	0.61
Residual		22	0.6	0	155.62	<0.001	0.6
Residual		31	0.58	0	146.33	<0.001	0.58
Residual		40	0.47	0.01	86.96	<0.001	0.47
Residual		48	0.42	0	90.21	<0.001	0.42
Residual		56	0.65	0	341.96	<0.001	0.65
Residual		61	0.41	0	186.35	<0.001	0.41
Residual		64	0.41	0	187.03	<0.001	0.41
Residual		5	0.3	0	100.35	<0.001	0.3
Residual		14	0.41	0	175.99	<0.001	0.41
Residual		23	0.2	0	88.12	<0.001	0.2
Residual		32	0.24	0	65.61	<0.001	0.24
Residual		67	0.13	0	49.7	<0.001	0.13
Residual		70	0.4	0	126.57	<0.001	0.4
Residual		74	0.41	0.01	67.66	<0.001	0.41
Residual		6	0.66	0.01	123.17	<0.001	0.66
Residual		15	0.41	0	125.71	<0.001	0.41
Residual		24	0.47	0	199.68	<0.001	0.47
Residual		33	0.42	0	164.12	<0.001	0.42
Residual		41	0.49	0	105.3	<0.001	0.49
Residual		49	0.81	0	275.09	<0.001	0.81
Residual		57	0.39	0	130.96	<0.001	0.39
Residual		62	0.68	0.01	126.78	<0.001	0.68
Residual		66	0.32	0	90.72	<0.001	0.32
Residual		7	0.46	0	180.43	<0.001	0.46
Residual		16	0.66	0	335.74	<0.001	0.66
Residual		25	0.64	0	224.88	<0.001	0.64
Residual		34	0.66	0	260.46	<0.001	0.66
Residual		42	0.4	0	122.08	<0.001	0.4
Residual		50	0.54	0	181.24	<0.001	0.54
Residual		58	0.51	0	223.93	<0.001	0.51

Table B.1 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Residual		69	0.34	0	113.47	<0.001	0.34
Residual		72	0.46	0	208.03	<0.001	0.46
Residual		8	0.44	0	191.55	<0.001	0.44
Residual		17	0.47	0	324.11	<0.001	0.47
Residual		26	0.43	0	110.25	<0.001	0.43
Residual		35	0.52	0	146.6	<0.001	0.52
Residual		43	0.42	0	87.42	<0.001	0.42
Residual		51	0.54	0	192.3	<0.001	0.54
Residual		68	0.64	0	246.38	<0.001	0.64
Residual		73	0.47	0	186.24	<0.001	0.47
Residual		9	0.42	0	171.71	<0.001	0.42
Residual		27	0.59	0	182.38	<0.001	0.59
Residual		36	0.3	0	71.22	<0.001	0.3
Residual		44	0.5	0	193.55	<0.001	0.5
Residual		52	0.44	0	142.06	<0.001	0.44
Residual		59	0.35	0	97.8	<0.001	0.35
Residual		65	0.52	0	244.49	<0.001	0.52
Variance	IOR	IOR	0.12	0.02	6.15	<0.001	1
Variance	SA	SA	0.59	0.03	19.61	<0.001	1
Variance	MT	MT	0.46	0.05	10.13	<0.001	1
Variance	UPE	UPE	0.39	0.03	13.77	<0.001	1
Variance	OB	OB	0.7	0.02	28.67	<0.001	1
Variance	NCF	NCF	0.34	0.03	10.13	<0.001	1
Variance	OS	OS	0.54	0.03	18.37	<0.001	1
Variance	CA	CA	0.56	0.03	19.93	<0.001	1
Variance	SUS	SUS	0.58	0.03	22.58	<0.001	1
Covariance	IOR	SA	0.13	0.01	10.47	<0.001	0.5
Covariance	IOR	MT	0.15	0.02	9.38	<0.001	0.63
Covariance	IOR	UPE	0.17	0.02	10.46	<0.001	0.76
Covariance	IOR	OB	0.16	0.01	10.72	<0.001	0.53
Covariance	IOR	NCF	0.1	0.01	9.3	<0.001	0.48
Covariance	IOR	OS	0.15	0.01	10.73	<0.001	0.6
Covariance	IOR	CA	0.14	0.01	10.47	<0.001	0.52
Covariance	IOR	SUS	0.23	0.02	11.63	<0.001	0.86
Covariance	SA	MT	0.11	0.02	6.81	<0.001	0.22
Covariance	SA	UPE	0.21	0.02	13.33	<0.001	0.43
Covariance	SA	OB	0.25	0.02	14.49	<0.001	0.4

Table B.1 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariance	SA	NCF	0.35	0.02	16.3	<0.001	0.77
Covariance	SA	OS	0.28	0.02	17.11	<0.001	0.5
Covariance	SA	CA	0.42	0.02	22.4	<0.001	0.73
Covariance	SA	SUS	0.34	0.02	19.76	<0.001	0.57
Covariance	MT	UPE	0.34	0.02	14.55	<0.001	0.8
Covariance	MT	OB	0.24	0.02	11.36	<0.001	0.42
Covariance	MT	NCF	0.09	0.01	6.43	<0.001	0.23
Covariance	MT	OS	0.22	0.02	11.51	<0.001	0.44
Covariance	MT	CA	0.15	0.02	7.99	<0.001	0.3
Covariance	MT	SUS	0.27	0.02	12.99	<0.001	0.52
Covariance	UPE	OB	0.33	0.02	18.4	<0.001	0.62
Covariance	UPE	NCF	0.17	0.01	11.63	<0.001	0.45
Covariance	UPE	OS	0.32	0.02	18.15	<0.001	0.69
Covariance	UPE	CA	0.26	0.02	15.89	<0.001	0.56
Covariance	UPE	SUS	0.34	0.02	19.06	<0.001	0.7
Covariance	OB	NCF	0.25	0.02	14.32	<0.001	0.51
Covariance	OB	OS	0.44	0.02	23.12	<0.001	0.73
Covariance	OB	CA	0.38	0.02	20.78	<0.001	0.61
Covariance	OB	SUS	0.37	0.02	21.03	<0.001	0.59
Covariance	NCF	OS	0.25	0.02	14.49	<0.001	0.57
Covariance	NCF	CA	0.42	0.02	17.35	<0.001	0.95
Covariance	NCF	SUS	0.32	0.02	16.6	<0.001	0.71
Covariance	OS	CA	0.4	0.02	21.89	<0.001	0.73
Covariance	OS	SUS	0.37	0.02	21.08	<0.001	0.65
Covariance	CA	SUS	0.41	0.02	23.15	<0.001	0.72

Table B.2: Pooled parameter estimates from the novel 6-factor SPQ model fit to 25 imputed datasets with a robust weighted-least-squares (WLSMV) estimator. Unstd. estimate ūnstandardised estimate. Std. estimate s̄tandardised estimate.

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	Aso	6	1	0	NA	NA	0.56
Loading	Aso	8	1.34	0.07	18.24	<0.001	0.75
Loading	Aso	15	1.31	0.07	18.32	<0.001	0.73
Loading	Aso	17	1.3	0.07	18.03	<0.001	0.72

Table B.2 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	Aso	24	1.25	0.07	18.07	<0.001	0.7
Loading	Aso	26	1.35	0.08	16.38	<0.001	0.76
Loading	Aso	33	1.3	0.07	18.16	<0.001	0.73
Loading	Aso	35	1.24	0.07	16.63	<0.001	0.69
Loading	Aso	41	1.22	0.07	17.14	<0.001	0.68
Loading	Aso	42	1.3	0.07	17.8	<0.001	0.73
Loading	Aso	43	1.35	0.07	18.6	<0.001	0.76
Loading	Aso	51	1.21	0.07	17.56	<0.001	0.68
Loading	Aso	52	1.32	0.08	17.61	<0.001	0.74
Loading	Aso	57	1.34	0.07	18.6	<0.001	0.75
Loading	Aso	62	0.97	0.07	14.07	<0.001	0.54
Loading	Aso	66	1.42	0.08	18.53	<0.001	0.79
Loading	Aso	68	1.08	0.07	15.59	<0.001	0.6
Loading	Aso	69	1.37	0.08	18.03	<0.001	0.76
Loading	Aso	73	1.3	0.07	17.53	<0.001	0.73
Loading	AEB	1	1	0	NA	NA	0.39
Loading	AEB	3	1.47	0.13	10.91	<0.001	0.57
Loading	AEB	4	1.7	0.14	12.17	<0.001	0.66
Loading	AEB	12	1.51	0.13	11.22	<0.001	0.58
Loading	AEB	13	1.72	0.14	12.26	<0.001	0.66
Loading	AEB	21	1.63	0.14	12.06	<0.001	0.63
Loading	AEB	22	1.72	0.17	10.32	<0.001	0.66
Loading	AEB	28	1.74	0.14	12.48	<0.001	0.67
Loading	AEB	30	1.38	0.13	10.73	<0.001	0.54
Loading	AEB	31	1.76	0.15	11.81	<0.001	0.68
Loading	AEB	37	1.72	0.14	12.41	<0.001	0.67
Loading	AEB	39	1.59	0.15	10.66	<0.001	0.62
Loading	AEB	40	1.98	0.17	11.47	<0.001	0.77
Loading	AEB	47	1.61	0.15	10.75	<0.001	0.62
Loading	AEB	55	1.68	0.15	10.94	<0.001	0.65
Loading	AEB	56	1.61	0.14	11.62	<0.001	0.62
Loading	AEB	61	2.08	0.17	12.42	<0.001	0.8
Loading	AEB	64	2.08	0.17	12.43	<0.001	0.8
Loading	PI	9	1	0	NA	NA	0.77
Loading	PI	10	0.72	0.03	21.95	<0.001	0.55
Loading	PI	19	0.91	0.03	29.47	<0.001	0.7
Loading	PI	27	0.84	0.03	27.56	<0.001	0.65

Table B.2 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	PI	36	1.09	0.03	34.55	<0.001	0.84
Loading	PI	44	0.93	0.03	30.11	<0.001	0.72
Loading	PI	45	0.87	0.03	27.6	<0.001	0.67
Loading	PI	48	0.94	0.04	21.68	<0.001	0.73
Loading	PI	53	0.97	0.03	35.35	<0.001	0.75
Loading	PI	59	1.05	0.03	31.97	<0.001	0.81
Loading	PI	60	1.03	0.03	34.82	<0.001	0.8
Loading	PI	63	1.03	0.03	40.85	<0.001	0.8
Loading	PI	65	0.9	0.03	28.22	<0.001	0.7
Loading	Ecc	5	1	0	NA	NA	0.83
Loading	Ecc	14	0.92	0.03	33.07	<0.001	0.76
Loading	Ecc	23	1.07	0.02	44.24	<0.001	0.89
Loading	Ecc	32	1.04	0.03	40.52	<0.001	0.87
Loading	Ecc	50	0.85	0.03	28.05	<0.001	0.7
Loading	Ecc	67	1.12	0.03	44.49	<0.001	0.92
Loading	Ecc	70	0.93	0.03	36.15	<0.001	0.77
Loading	Ecc	74	0.92	0.04	22.23	<0.001	0.76
Loading	SA	2	1	0	NA	NA	0.77
Loading	SA	11	1.06	0.03	30.23	<0.001	0.81
Loading	SA	20	0.71	0.04	18.9	<0.001	0.54
Loading	SA	29	1.03	0.03	31.04	<0.001	0.79
Loading	SA	38	1.09	0.03	31.69	<0.001	0.84
Loading	SA	46	1.21	0.03	36.07	<0.001	0.93
Loading	SA	54	0.57	0.04	13.89	<0.001	0.44
Loading	SA	71	1.19	0.03	34.9	<0.001	0.91
Loading	OS	7	1	0	NA	NA	0.8
Loading	OS	16	0.8	0.04	20.59	<0.001	0.64
Loading	OS	25	0.82	0.04	20.6	<0.001	0.65
Loading	OS	34	0.81	0.04	20.72	<0.001	0.64
Loading	OS	58	0.96	0.04	24.83	<0.001	0.77
Loading	OS	72	1.01	0.04	24.97	<0.001	0.81
Threshold	0 -> 1	6	1.05	0.03	33.13	<0.001	1.05
Threshold	0 -> 1	8	0.53	0.03	19.64	<0.001	0.53
Threshold	0 -> 1	15	0.12	0.03	4.77	<0.001	0.12
Threshold	0 -> 1	17	0.15	0.03	5.81	<0.001	0.15
Threshold	0 -> 1	24	0.51	0.03	19.03	<0.001	0.51
Threshold	0 -> 1	26	1.5	0.04	37.79	<0.001	1.5

Table B.2 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Threshold	0 -> 1	33	0.46	0.03	17.08	<0.001	0.46
Threshold	0 -> 1	35	1.12	0.03	34.37	<0.001	1.12
Threshold	0 -> 1	41	0.83	0.03	28.33	<0.001	0.83
Threshold	0 -> 1	42	0.91	0.03	30.23	<0.001	0.91
Threshold	0 -> 1	43	0.98	0.03	31.9	<0.001	0.98
Threshold	0 -> 1	51	0.7	0.03	24.93	<0.001	0.7
Threshold	0 -> 1	52	-0.03	0.03	-1.01	0.031	-0.03
Threshold	0 -> 1	57	0.33	0.03	12.42	<0.001	0.33
Threshold	0 -> 1	62	1.35	0.04	37.09	<0.001	1.35
Threshold	0 -> 1	66	0.76	0.03	26.66	<0.001	0.76
Threshold	0 -> 1	68	0.85	0.03	28.96	<0.001	0.85
Threshold	0 -> 1	69	0.66	0.03	23.84	<0.001	0.66
Threshold	0 -> 1	73	-0.23	0.03	-9.03	<0.001	-0.23
Threshold	0 -> 1	1	0.24	0.03	9.31	<0.001	0.24
Threshold	0 -> 1	3	1.12	0.03	34.37	<0.001	1.12
Threshold	0 -> 1	4	0.15	0.03	5.73	<0.001	0.15
Threshold	0 -> 1	12	1.11	0.03	34.17	<0.001	1.11
Threshold	0 -> 1	13	0.51	0.03	18.9	<0.001	0.51
Threshold	0 -> 1	21	0.77	0.03	26.89	<0.001	0.77
Threshold	0 -> 1	22	1.49	0.04	37.86	<0.001	1.49
Threshold	0 -> 1	28	0.81	0.03	27.94	<0.001	0.81
Threshold	0 -> 1	30	1.02	0.03	32.52	<0.001	1.02
Threshold	0 -> 1	31	0.99	0.03	32.16	<0.001	0.99
Threshold	0 -> 1	37	1.17	0.03	35.24	<0.001	1.17
Threshold	0 -> 1	39	1.5	0.04	37.85	<0.001	1.5
Threshold	0 -> 1	40	1.39	0.04	37.33	<0.001	1.39
Threshold	0 -> 1	47	1.33	0.04	36.97	<0.001	1.33
Threshold	0 -> 1	55	1.45	0.04	37.76	<0.001	1.45
Threshold	0 -> 1	56	0.79	0.03	27.33	<0.001	0.79
Threshold	0 -> 1	61	0.49	0.03	18.39	<0.001	0.49
Threshold	0 -> 1	64	0.66	0.03	23.67	<0.001	0.66
Threshold	0 -> 1	9	0.25	0.03	9.77	<0.001	0.25
Threshold	0 -> 1	10	0.18	0.03	7.13	<0.001	0.18
Threshold	0 -> 1	19	0.6	0.03	21.83	<0.001	0.6
Threshold	0 -> 1	27	-0.05	0.03	-2.12	0.013	-0.05
Threshold	0 -> 1	36	0.62	0.03	22.51	<0.001	0.62
Threshold	0 -> 1	44	0.56	0.03	20.52	<0.001	0.56

Table B.2 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Threshold	0 -> 1	45	0.4	0.03	15.03	<0.001	0.4
Threshold	0 -> 1	48	1.37	0.04	37.22	<0.001	1.37
Threshold	0 -> 1	53	0.37	0.03	14.01	<0.001	0.37
Threshold	0 -> 1	59	1.03	0.03	32.89	<0.001	1.03
Threshold	0 -> 1	60	0.39	0.03	14.7	<0.001	0.39
Threshold	0 -> 1	63	0.16	0.03	6.2	<0.001	0.16
Threshold	0 -> 1	65	0.57	0.03	20.99	<0.001	0.57
Threshold	0 -> 1	5	0.28	0.03	10.68	<0.001	0.28
Threshold	0 -> 1	14	0.47	0.03	17.45	<0.001	0.47
Threshold	0 -> 1	23	0.05	0.03	1.94	0.05	0.05
Threshold	0 -> 1	32	0.8	0.03	27.53	<0.001	0.8
Threshold	0 -> 1	50	0.34	0.03	13.09	<0.001	0.34
Threshold	0 -> 1	67	0.6	0.03	21.82	<0.001	0.6
Threshold	0 -> 1	70	0.43	0.03	16.17	<0.001	0.43
Threshold	0 -> 1	74	1.36	0.04	37.22	<0.001	1.36
Threshold	0 -> 1	2	0.39	0.03	14.68	<0.001	0.39
Threshold	0 -> 1	11	0.56	0.03	20.5	<0.001	0.56
Threshold	0 -> 1	20	-0.06	0.03	-2.45	0.01	-0.06
Threshold	0 -> 1	29	-0.2	0.03	-7.87	<0.001	-0.2
Threshold	0 -> 1	38	-0.33	0.03	-12.6	<0.001	-0.33
Threshold	0 -> 1	46	0.27	0.03	10.45	<0.001	0.27
Threshold	0 -> 1	54	-0.55	0.03	-20.3	<0.001	-0.55
Threshold	0 -> 1	71	0.32	0.03	12.12	<0.001	0.32
Threshold	0 -> 1	7	0.45	0.03	16.73	<0.001	0.45
Threshold	0 -> 1	16	-0.12	0.03	-4.82	<0.001	-0.12
Threshold	0 -> 1	25	-0.27	0.03	-10.2	<0.001	-0.27
Threshold	0 -> 1	34	0.08	0.03	3.09	<0.001	0.08
Threshold	0 -> 1	58	0.18	0.03	7.04	<0.001	0.18
Threshold	0 -> 1	72	0.9	0.03	30.2	<0.001	0.9
Residual		6	0.69	0	141.5	<0.001	0.69
Residual		8	0.44	0	181.8	<0.001	0.44
Residual		15	0.46	0	151.5	<0.001	0.46
Residual		17	0.48	0	309.6	<0.001	0.48
Residual		24	0.51	0	234.5	<0.001	0.51
Residual		26	0.43	0	123.5	<0.001	0.43
Residual		33	0.47	0	198.9	<0.001	0.47
Residual		35	0.52	0	149.9	<0.001	0.52

Table B.2 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Residual		41	0.53	0	120.6	<0.001	0.53
Residual		42	0.47	0	165.1	<0.001	0.47
Residual		43	0.43	0	99.32	<0.001	0.43
Residual		51	0.54	0	195.6	<0.001	0.54
Residual		52	0.45	0	164.5	<0.001	0.45
Residual		57	0.44	0	153.7	<0.001	0.44
Residual		62	0.71	0.01	140.6	<0.001	0.71
Residual		66	0.37	0	108.8	<0.001	0.37
Residual		68	0.64	0	279.9	<0.001	0.64
Residual		69	0.42	0	155.4	<0.001	0.42
Residual		73	0.47	0	196.5	<0.001	0.47
Residual		1	0.85	0	643.9	<0.001	0.85
Residual		3	0.68	0	194.6	<0.001	0.68
Residual		4	0.57	0	217	<0.001	0.57
Residual		12	0.66	0	173.5	<0.001	0.66
Residual		13	0.56	0	228.7	<0.001	0.56
Residual		21	0.6	0	230.5	<0.001	0.6
Residual		22	0.56	0	136.9	<0.001	0.56
Residual		28	0.55	0	164.4	<0.001	0.55
Residual		30	0.71	0	193	<0.001	0.71
Residual		31	0.54	0	130.8	<0.001	0.54
Residual		37	0.56	0	134.6	<0.001	0.56
Residual		39	0.62	0.01	111.4	<0.001	0.62
Residual		40	0.41	0.01	70.43	<0.001	0.41
Residual		47	0.61	0	206.3	<0.001	0.61
Residual		55	0.58	0	122.6	<0.001	0.58
Residual		56	0.61	0	286.4	<0.001	0.61
Residual		61	0.35	0	148.3	<0.001	0.35
Residual		64	0.35	0	149.1	<0.001	0.35
Residual		9	0.4	0	195.5	<0.001	0.4
Residual		10	0.69	0	403.9	<0.001	0.69
Residual		19	0.51	0	173.6	<0.001	0.51
Residual		27	0.57	0	180.3	<0.001	0.57
Residual		36	0.29	0	71.36	<0.001	0.29
Residual		44	0.48	0	186.9	<0.001	0.48
Residual		45	0.55	0	170.2	<0.001	0.55
Residual		48	0.47	0.01	93.5	<0.001	0.47

Table B.2 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Residual		53	0.44	0	175.1	<0.001	0.44
Residual		59	0.34	0	100.7	<0.001	0.34
Residual		60	0.37	0	173.2	<0.001	0.37
Residual		63	0.37	0	127.2	<0.001	0.37
Residual		65	0.51	0	227.8	<0.001	0.51
Residual		5	0.31	0	104.1	<0.001	0.31
Residual		14	0.42	0	178.1	<0.001	0.42
Residual		23	0.21	0	91.06	<0.001	0.21
Residual		32	0.25	0	66.73	<0.001	0.25
Residual		50	0.5	0	159.7	<0.001	0.5
Residual		67	0.15	0	56.18	<0.001	0.15
Residual		70	0.41	0	129.9	<0.001	0.41
Residual		74	0.42	0.01	70.78	<0.001	0.42
Residual		2	0.41	0	185.9	<0.001	0.41
Residual		11	0.34	0	115.7	<0.001	0.34
Residual		20	0.7	0	330.8	<0.001	0.7
Residual		29	0.37	0	137.8	<0.001	0.37
Residual		38	0.29	0	124.1	<0.001	0.29
Residual		46	0.14	0	54.45	<0.001	0.14
Residual		54	0.81	0	415.4	<0.001	0.81
Residual		71	0.16	0	62.57	<0.001	0.16
Residual		7	0.36	0	119.6	<0.001	0.36
Residual		16	0.59	0	255.3	<0.001	0.59
Residual		25	0.57	0	177.5	<0.001	0.57
Residual		34	0.58	0	215	<0.001	0.58
Residual		58	0.4	0	162.3	<0.001	0.4
Residual		72	0.35	0	137.3	<0.001	0.35
Variance	Aso	Aso	0.31	0.03	9.84	<0.001	1
Variance	AEB	AEB	0.15	0.02	6.63	<0.001	1
Variance	PI	PI	0.6	0.03	23.86	<0.001	1
Variance	Ecc	Ecc	0.69	0.02	28.39	<0.001	1
Variance	SA	SA	0.59	0.03	19.58	<0.001	1
Variance	OS	OS	0.64	0.04	17.62	<0.001	1
Covariance	Aso	AEB	0.1	0.01	9.4	<0.001	0.44
Covariance	Aso	PI	0.28	0.02	15.87	<0.001	0.64
Covariance	Aso	Ecc	0.27	0.02	15.47	<0.001	0.58
Covariance	Aso	SA	0.32	0.02	15.84	<0.001	0.75

Table B.2 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariance	Aso	OS	0.25	0.02	14.72	<0.001	0.57
Covariance	AEB	PI	0.2	0.02	11.77	<0.001	0.68
Covariance	AEB	Ecc	0.19	0.02	11.73	<0.001	0.58
Covariance	AEB	SA	0.1	0.01	9.37	<0.001	0.35
Covariance	AEB	OS	0.17	0.02	11.23	<0.001	0.56
Covariance	PI	Ecc	0.37	0.02	22.12	<0.001	0.58
Covariance	PI	SA	0.33	0.02	20.03	<0.001	0.56
Covariance	PI	OS	0.37	0.02	20.93	<0.001	0.6
Covariance	Ecc	SA	0.25	0.02	14.32	<0.001	0.39
Covariance	Ecc	OS	0.45	0.02	22.67	<0.001	0.69
Covariance	SA	OS	0.27	0.02	15.11	<0.001	0.43
Covariance	SA	UPE	0.21	0.02	13.33	0.001	0.43
Covariance	SA	OB	0.25	0.02	14.49	0.001	0.4
Covariance	SA	NCF	0.35	0.02	16.3	0.001	0.77
Covariance	SA	OS	0.28	0.02	17.11	0.001	0.5
Covariance	SA	CA	0.42	0.02	22.4	0.001	0.73
Covariance	SA	SUS	0.34	0.02	19.76	0.001	0.57
Covariance	MT	UPE	0.34	0.02	14.55	0.001	0.8
Covariance	MT	OB	0.24	0.02	11.36	0.001	0.42
Covariance	MT	NCF	0.09	0.01	6.43	0.001	0.23
Covariance	MT	OS	0.22	0.02	11.51	0.001	0.44
Covariance	MT	CA	0.15	0.02	7.99	0.001	0.3
Covariance	MT	SUS	0.27	0.02	12.99	0.001	0.52
Covariance	UPE	OB	0.33	0.02	18.4	0.001	0.62
Covariance	UPE	NCF	0.17	0.01	11.63	0.001	0.45
Covariance	UPE	OS	0.32	0.02	18.15	0.001	0.69
Covariance	UPE	CA	0.26	0.02	15.89	0.001	0.56
Covariance	UPE	SUS	0.34	0.02	19.06	0.001	0.7
Covariance	OB	NCF	0.25	0.02	14.32	0.001	0.51
Covariance	OB	OS	0.44	0.02	23.12	0.001	0.73
Covariance	OB	CA	0.38	0.02	20.78	0.001	0.61
Covariance	OB	SUS	0.37	0.02	21.03	0.001	0.59
Covariance	NCF	OS	0.25	0.02	14.49	0.001	0.57
Covariance	NCF	CA	0.42	0.02	17.35	0.001	0.95
Covariance	NCF	SUS	0.32	0.02	16.6	0.001	0.71
Covariance	OS	CA	0.4	0.02	21.89	0.001	0.73
Covariance	OS	SUS	0.37	0.02	21.08	0.001	0.65

Table B.2 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariance	CA	SUS	0.41	0.02	23.15	0.001	0.72

Table B.3: Parameter estimates from the 3-factor model of the BSSI fit to 5-category data using a robust maximum likelihood estimator, with missing value estimated using full-information maximum likelihood.

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	SA	1	1	0	NA	NA	0.55
Loading	SA	4	1.24	0.08	15.52	<0.001	0.65
Loading	SA	7	1.85	0.12	15.3	<0.001	0.86
Loading	SA	11	1.93	0.13	15.39	<0.001	0.9
Loading	SA	14	1.8	0.12	15.13	<0.001	0.88
Loading	SA	17	1.83	0.12	14.76	<0.001	0.85
Loading	AEB	2	1	0	NA	NA	0.73
Loading	AEB	5	0.84	0.08	10.65	<0.001	0.62
Loading	AEB	8	0.57	0.08	7.08	<0.001	0.55
Loading	AEB	10	0.41	0.07	5.53	<0.001	0.35
Loading	AEB	13	0.33	0.07	4.67	<0.001	0.48
Loading	AEB	16	0.39	0.06	6.88	<0.001	0.5
Loading	AEB	18	1.04	0.06	16.65	<0.001	0.73
Loading	AEB	20	0.36	0.05	6.78	<0.001	0.54
Loading	PI	3	1	0	NA	NA	0.77
Loading	PI	9	0.91	0.06	14.41	<0.001	0.78
Loading	PI	12	0.68	0.05	13.45	<0.001	0.7
Loading	PI	15	1.11	0.06	19.25	<0.001	0.91
Loading	PI	19	0.63	0.05	11.5	<0.001	0.56
Residual		1	0.59	0.04	15.19	<0.001	0.7
Residual		4	0.53	0.04	14.29	<0.001	0.57
Residual		7	0.3	0.02	12.39	<0.001	0.25
Residual		11	0.23	0.02	13.15	<0.001	0.2
Residual		14	0.23	0.03	7.72	<0.001	0.22
Residual		17	0.33	0.03	12.44	<0.001	0.28
Residual		2	0.34	0.04	8.07	<0.001	0.47
Residual		5	0.44	0.05	9.37	<0.001	0.61
Residual		8	0.3	0.03	9.74	<0.001	0.7

Table B.3 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Residual		10	0.47	0.06	8.31	<0.001	0.88
Residual		13	0.15	0.02	7.06	<0.001	0.77
Residual		16	0.18	0.03	7.06	<0.001	0.75
Residual		18	0.38	0.05	7.97	<0.001	0.47
Residual		20	0.12	0.02	5.38	<0.001	0.71
Residual		3	0.38	0.04	10.55	<0.001	0.41
Residual		9	0.3	0.02	12.79	<0.001	0.4
Residual		12	0.27	0.02	13.34	<0.001	0.51
Residual		15	0.14	0.02	7.58	<0.001	0.17
Residual		19	0.47	0.04	12.22	<0.001	0.68
Variances	SA	SA	0.25	0.03	7.25	<0.001	1
Variances	AEB	AEB	0.39	0.06	6.98	<0.001	1
Variances	PI	PI	0.56	0.06	9.76	<0.001	1
Covariances	SA	AEB	0.08	0.01	5.53	<0.001	0.26
Covariances	SA	PI	0.18	0.02	7.57	<0.001	0.48
Covariances	AEB	PI	0.21	0.03	7.65	<0.001	0.44
Intercepts		1	1.56	0.03	52.78	<0.001	1.7
Intercepts		4	1.66	0.03	53.94	<0.001	1.74
Intercepts		7	1.91	0.03	55.19	<0.001	1.78
Intercepts		11	2.08	0.03	59.97	<0.001	1.93
Intercepts		14	1.83	0.03	55.79	<0.001	1.8
Intercepts		17	2.06	0.03	59.34	<0.001	1.91
Intercepts		2	1.46	0.03	52.68	<0.001	1.7
Intercepts		5	1.41	0.03	51.5	<0.001	1.66
Intercepts		8	1.26	0.02	59.69	<0.001	1.93
Intercepts		10	1.26	0.02	53.08	<0.001	1.72
Intercepts		13	1.12	0.01	78.84	<0.001	2.57
Intercepts		16	1.16	0.02	73.14	<0.001	2.38
Intercepts		18	1.45	0.03	50.15	<0.001	1.62
Intercepts		20	1.1	0.01	81.56	<0.001	2.63
Intercepts		3	1.95	0.03	62.34	<0.001	2.01
Intercepts		9	1.61	0.03	57.06	<0.001	1.84
Intercepts		12	1.36	0.02	57.85	<0.001	1.87
Intercepts		15	1.75	0.03	59.58	<0.001	1.92
Intercepts		19	1.54	0.03	57.3	<0.001	1.85

Table B.3

Table B.4: Pooled parameter estimates from the BSSI 3-factor model, fit to 25 imputed datasets with a robust weighted-least-squares (WLSMV) estimator. Unstd. estimate ūnstandardised estimate. Std. estimate s̄tandardised estimate.

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	SA	1	1	0	NA	NA	0.66
Loading	SA	4	1.08	0.05	20.93	0	0.72
Loading	SA	7	1.29	0.06	22.88	0	0.85
Loading	SA	11	1.38	0.06	23.96	0	0.92
Loading	SA	14	1.38	0.06	23.52	0	0.92
Loading	SA	17	1.31	0.06	22.83	0	0.87
Loading	AEB	2	1	0	NA	NA	0.81
Loading	AEB	5	0.95	0.05	18.51	0	0.76
Loading	AEB	8	0.83	0.05	15.54	0	0.67
Loading	AEB	10	0.76	0.06	12.37	0	0.61
Loading	AEB	13	0.96	0.06	16.34	0	0.77
Loading	AEB	16	0.84	0.06	13.31	0	0.68
Loading	AEB	18	0.98	0.05	21.68	0	0.79
Loading	AEB	20	0.93	0.06	15.35	0	0.75
Loading	PI	3	1	0	NA	NA	0.78
Loading	PI	9	1.04	0.04	26.69	0	0.81
Loading	PI	12	0.99	0.04	25.33	0	0.77
Loading	PI	15	1.16	0.04	30.65	0	0.91
Loading	PI	19	0.93	0.04	21.39	0	0.73
Threshold	0->1	1	0.43	0.04	9.78	0	0.43
Threshold	1->2	1	0.96	0.05	19.65	0	0.96
Threshold	0->1	4	0.23	0.04	5.93	0	0.23
Threshold	1->2	4	0.95	0.05	19.96	0	0.94
Threshold	0->1	7	-0.11	0.04	-2.68	0.01	-0.11
Threshold	1->2	7	0.73	0.05	16.1	0	0.73
Threshold	0->1	11	-0.41	0.04	-9.73	0	-0.41
Threshold	1->2	11	0.6	0.04	13.4	0	0.6
Threshold	0->1	14	-0.07	0.04	-1.73	0.08	-0.07
Threshold	1->2	14	0.87	0.05	18.28	0	0.87
Threshold	0->1	17	-0.41	0.04	-10.03	0	-0.41
Threshold	1->2	17	0.7	0.04	15.89	0	0.7
Threshold	0->1	2	0.58	0.04	14	0	0.58
Threshold	1->2	2	1.15	0.05	23.24	0	1.15
Threshold	0->1	5	0.67	0.04	15.08	0	0.67
Threshold	1->2	5	1.26	0.06	21.92	0	1.26

Table B.4 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Threshold	0->1	8	0.96	0.05	20.94	0	0.96
Threshold	1->2	8	1.5	0.06	24.14	0	1.5
Threshold	0->1	10	1.06	0.05	22.09	0	1.06
Threshold	1->2	10	1.49	0.06	23.53	0	1.49
Threshold	0->1	13	1.34	0.06	22.14	0	1.34
Threshold	1->2	13	1.95	0.09	21.54	0	1.95
Threshold	0->1	16	1.19	0.05	21.93	0	1.19
Threshold	1->2	16	1.89	0.08	24.69	0	1.89
Threshold	0->1	18	0.62	0.04	15.24	0	0.62
Threshold	1->2	18	1.22	0.05	23.43	0	1.22
Threshold	0->1	20	1.49	0.06	24.03	0	1.49
Threshold	1->2	20	2.01	0.09	23.13	0	2.01
Threshold	0->1	3	-0.33	0.04	-8.19	0	-0.33
Threshold	1->2	3	0.78	0.04	17.73	0	0.78
Threshold	0->1	9	0.2	0.04	4.73	0	0.2
Threshold	1->2	9	1.11	0.05	23.2	0	1.11
Threshold	0->1	12	0.69	0.05	14.83	0	0.69
Threshold	1->2	12	1.43	0.06	23.68	0	1.43
Threshold	0->1	15	-0.05	0.04	-1.36	0.17	-0.05
Threshold	1->2	15	1.01	0.05	21.25	0	1.01
Threshold	0->1	19	0.32	0.04	7.58	0	0.32
Threshold	1->2	19	1.17	0.05	22.77	0	1.17
Residual		1	0.56	0.01	42.6	0	0.56
Residual		4	0.48	0.02	27.58	0	0.48
Residual		7	0.27	0.01	19.51	0	0.27
Residual		11	0.16	0.01	16.55	0	0.16
Residual		14	0.16	0.01	15.82	0	0.16
Residual		17	0.24	0.01	16.73	0	0.24
Residual		2	0.35	0.02	14.76	0	0.35
Residual		5	0.42	0.03	15.15	0	0.42
Residual		8	0.55	0.02	22.96	0	0.55
Residual		10	0.62	0.02	35.02	0	0.62
Residual		13	0.4	0.03	14.66	0	0.4
Residual		16	0.54	0.04	15.32	0	0.54
Residual		18	0.37	0.02	17.6	0	0.37
Residual		20	0.44	0.03	16.32	0	0.44
Residual		3	0.39	0.02	23.72	0	0.39

Table B.4 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Residual		9	0.34	0.02	18.76	0	0.34
Residual		12	0.4	0.01	29.2	0	0.4
Residual		15	0.18	0.01	16.94	0	0.18
Residual		19	0.47	0.02	25.03	0	0.47
Variance	SA	SA	0.44	0.04	12.08	0	1
Variance	AEB	AEB	0.65	0.04	15.13	0	1
Variance	PI	PI	0.61	0.03	18.1	0	1
Covariance	SA	AEB	0.18	0.02	7.87	0	0.33
Covariance	SA	PI	0.25	0.02	11.99	0	0.48
Covariance	AEB	PI	0.36	0.02	14.67	0	0.57

B.2 Parameter estimates of models from Chapter 5

Table B.5: Parameter estimates from 9-factor SPQ model (WLSMV, 25 imputed datasets)

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	GF	Delusions (Interview)	1	0	NA	NA	0.62
Loading	GF	Anomalous Experiences (Interview)	0.65	0.15	4.23	0	0.4
Loading	GF	Hallucinations (Interview)	1	0.13	7.97	0	0.62
Loading	GF	Believe In Telepathy	1.31	0.13	9.79	0	0.81
Loading	GF	Force Around You	1.21	0.12	9.75	0	0.75
Loading	GF	See Special Signs	1.13	0.11	10.01	0	0.7
Loading	GF	Hear Voice Speaking Thoughts	0.92	0.11	8.56	0	0.57
Loading	GF	See Invisible Things	1.2	0.13	9.01	0	0.74

Table B.5 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	GF	Others Feel Your Feelings	1.13	0.11	9.93	0	0.7
Loading	GF	Believe In Clairvoyancy	1.32	0.13	10.16	0	0.81
Loading	GF	Telepathic Experiences	1.26	0.13	9.63	0	0.78
Loading	GF	Talked About Behind Back	0.93	0.14	6.71	0	0.58
Loading	GF	People Talk About You	0.82	0.15	5.49	0	0.51
Loading	GF	Others Have It In For You	0.92	0.14	6.5	0	0.57
Loading	GF	Others Often Talk About You	0.89	0.17	5.35	0	0.55
Loading	GF	People Watch You	1.11	0.12	8.95	0	0.68
Loading	SF1	Hallucinations	1	0	NA	NA	0.5
Loading	SF1	Delusions	1.56	1	1.55	0.12	0.78
Loading	SF1	Anomalous Experiences	0.55	0.29	1.89	0.06	0.28
Loading	SF2	Believe In Telepathy	1	0	NA	NA	0.27
Loading	SF2	Force Around You	-0.15	0.29	-0.53	0.6	-0.04
Loading	SF2	See Special Signs	0.23	0.23	1.01	0.31	0.06
Loading	SF2	Hear Voice Speaking Thoughts	-0.32	0.32	-1	0.32	-0.09
Loading	SF2	See Invisible Things	-0.23	0.35	-0.67	0.5	-0.06
Loading	SF2	Others Feel Your Feelings	0.26	0.24	1.05	0.29	0.07
Loading	SF2	Believe In Clairvoyancy	1.17	0.19	6.12	0	0.32

Table B.5 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	SF2	Telepathic Experiences	0.9	0.22	4.08	0	0.25
Loading	SF2	Talked About Behind Back	-2.03	0.76	-2.66	0.01	-0.56
Loading	SF2	People Talk About You	-2.36	0.84	-2.81	0	-0.65
Loading	SF2	Others Have It In For You	-2.01	0.77	-2.62	0.01	-0.55
Loading	SF2	Others Often Talk About You	-3	1.05	-2.86	0	-0.82
Loading	SF2	People Watch You	-1.03	0.51	-2.02	0.04	-0.28
Threshold	0->1	Hallucinations	1.62	0.07	23.63	0	1.62
Threshold	0->1	Delusions	1.96	0.09	22.25	0	1.96
Threshold	0->1	Anomalous Experiences	1.55	0.07	23.65	0	1.55
Threshold	0->1	Believe In Telepathy	0.61	0.04	13.76	0	0.61
Threshold	1->2	Force Around You	1.17	0.05	21.92	0	1.17
Threshold	0->1	See Special Signs	0.69	0.05	15.28	0	0.69
Threshold	1->2	Hear Voice Speaking Thoughts	1.26	0.06	22.58	0	1.26
Threshold	0->1	See Invisible Things	0.97	0.05	19.64	0	0.97
Threshold	1->2	Others Feel Your Feelings	1.48	0.06	23.56	0	1.48
Threshold	0->1	Believe In Clairvoyancy	1.08	0.05	21.07	0	1.08
Threshold	1->2	Telepathic Experiences	1.5	0.06	23.59	0	1.5
Threshold	0->1	Talked About Behind Back	1.39	0.06	23.29	0	1.39

Table B.5 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Threshold	1->2	People Talk About You	1.96	0.09	22.25	0	1.96
Threshold	0->1	Others Have It In For You	1.21	0.05	22.24	0	1.21
Threshold	1->2	Others Often Talk About You	1.89	0.08	22.7	0	1.89
Threshold	0->1	People Watch You	0.63	0.04	14.27	0	0.63
Threshold	1->2	t2	1.22	0.05	22.28	0	1.22
Threshold	0->1	t1	1.54	0.07	23.65	0	1.54
Threshold	1->2	t2	2.02	0.09	21.82	0	2.02
Threshold	0->1	t1	-0.3	0.04	-7.2	0	-0.3
Threshold	1->2	t2	0.8	0.05	17.21	0	0.8
Threshold	0->1	t1	0.24	0.04	5.69	0	0.24
Threshold	1->2	t2	1.12	0.05	21.43	0	1.12
Threshold	0->1	t1	0.72	0.05	15.78	0	0.72
Threshold	1->2	t2	1.46	0.06	23.51	0	1.46
Threshold	0->1	t1	-0.03	0.04	-0.69	0.49	-0.03
Threshold	1->2	t2	1.01	0.05	20.15	0	1.01
Threshold	0->1	t1	0.34	0.04	8.12	0	0.34
Threshold	1->2	t2	1.19	0.05	22.06	0	1.19
Residual		Delusions	0.36	0	NA	NA	0.36
Residual		Anomalous Experiences	0.23	0	NA	NA	0.23
Residual		Hallucinations	0.54	0	NA	NA	0.54
Residual		Believe In Telepathy	0.26	0	NA	NA	0.26
Residual		Force Around You	0.43	0	NA	NA	0.43
Residual		See Special Signs	0.5	0	NA	NA	0.5
Residual		Hear Voice Speaking Thoughts	0.67	0	NA	NA	0.67
Residual		See Invisible Things	0.44	0	NA	NA	0.44

Table B.5 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Residual		Others Feel Your Feelings	0.5	0	NA	NA	0.5
Residual		Believe In Clairvoyancy	0.23	0	NA	NA	0.23
Residual		Telepathic Experiences	0.33	0	NA	NA	0.33
Residual		Talked About Behind Back	0.36	0	NA	NA	0.36
Residual		People Talk About You	0.33	0	NA	NA	0.33
Residual		Others Have It In For You	0.37	0	NA	NA	0.37
Residual		Others Often Talk About You	0.03	0	NA	NA	0.03
Residual		People Watch You	0.45	0	NA	NA	0.45
Variance	General Factor	General Factor	0.38	0.08	5	0	1
Variance	Specific Factor 1	Specific Factor 1	0.25	0.17	1.47	0.14	1
Variance	Specific Factor 2	Specific Factor 2	0.07	0.04	1.7	0.09	1
Covariance	General Factor	Specific Factor 1	0	0	NA	NA	0
Covariance	General Factor	Specific Factor 2	0	0	NA	NA	0
Covariance	Specific Factor 1	Specific Factor 2	0	0	NA	NA	0

Table B.5: Parameter estimates from bifactor model fit to combined PLIKSi and BSSI items with a robust weighted-least-squares (WLSMV) estimator. GF = general factor. SF1 = specific PLIKSi factor. SF2 = specific BSSI factor. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate. t1 = First item threshold. t2 = Second item threshold (BSSI only).

B.3 Parameter estimates from structural equation models in Chapter 8

Table B.6: Parameter estimates from cross-lagged models of Asociality and Anomalous Experiences & Beliefs

Parameter type	Factor or threshold	Item or factor	Equality constraint	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	ASO (BL)	ASO: Parcel 1 (BL)	l7	1	0	NA	NA	0.75
Loading	ASO (BL)	ASO: Parcel 2 (BL)	l8	0.94	0.02	46.06	< 0.001	0.76
Loading	ASO (BL)	ASO: Parcel 3 (BL)	l9	0.92	0.02	39.21	< 0.001	0.74
Loading	ASO (BL)	ASO: Parcel 4 (BL)	l10	0.86	0.02	38.1	< 0.001	0.7
Loading	ASO (BL)	ASO: Parcel 5 (BL)	l11	0.95	0.02	46.96	< 0.001	0.75
Loading	ASO (BL)	ASO: Parcel 6 (BL)	l12	1.41	0.03	46.25	< 0.001	0.83
Loading	ASO (FU)	ASO: Parcel 1 (FU)	l7	1	0	NA	NA	0.75
Loading	ASO (FU)	ASO: Parcel 2 (FU)	l8	0.94	0.02	46.06	< 0.001	0.77
Loading	ASO (FU)	ASO: Parcel 3 (FU)	l9	0.92	0.02	39.21	< 0.001	0.75
Loading	ASO (FU)	ASO: Parcel 4 (FU)	l10	0.86	0.02	38.1	< 0.001	0.71
Loading	ASO (FU)	ASO: Parcel 5 (FU)	l11	0.95	0.02	46.96	< 0.001	0.76
Loading	ASO (FU)	ASO: Parcel 6 (FU)	l12	1.41	0.03	46.25	< 0.001	0.83
Loading	AEB (BL)	AEB: Parcel 1 (BL)	l1	1	0	NA	NA	0.64
Loading	AEB (BL)	AEB: Parcel 2 (BL)	l2	1.11	0.03	32.07	< 0.001	0.75
Loading	AEB (BL)	AEB: Parcel 3 (BL)	l3	0.86	0.03	26.18	< 0.001	0.7
Loading	AEB (BL)	AEB: Parcel 4 (BL)	l4	0.69	0.03	22.57	< 0.001	0.65
Loading	AEB (BL)	AEB: Parcel 5 (BL)	l5	0.65	0.03	20.68	< 0.001	0.66
Loading	AEB (BL)	AEB: Parcel 6 (BL)	l6	1.15	0.04	29.3	< 0.001	0.69
Loading	AEB (FU)	AEB: Parcel 1 (FU)	l1	1	0	NA	NA	0.6

Table B.6 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	AEB (FU)	AEB: Parcel 2 (FU)	l2	1.11	0.03	32.07	< 0.001	0.71
Loading	AEB (FU)	AEB: Parcel 3 (FU)	l3	0.86	0.03	26.18	< 0.001	0.66
Loading	AEB (FU)	AEB: Parcel 4 (FU)	l4	0.69	0.03	22.57	< 0.001	0.61
Loading	AEB (FU)	AEB: Parcel 5 (FU)	l5	0.65	0.03	20.68	< 0.001	0.62
Loading	AEB (FU)	AEB: Parcel 6 (FU)	l6	1.15	0.04	29.3	< 0.001	0.65
Regression	ASO (FU)	ASO (BL)		0.84	0.02	39.58	< 0.001	0.83
Regression	ASO (FU)	AEB (BL)		-0.04	0.03	-1.34	0.181	-0.03
Regression	AEB (FU)	AEB (BL)		0.63	0.03	18.56	< 0.001	0.7
Regression	AEB (FU)	ASO (BL)		0.04	0.02	2	0.046	0.05
Intercept	AEB: Parcel 1 (BL)		ia1	1.04	0.13	7.83	< 0.001	1.18
Intercept	AEB: Parcel 2 (BL)		ia2	0.77	0.15	5.21	< 0.001	0.92
Intercept	AEB: Parcel 3 (BL)		ia3	0.53	0.11	4.6	< 0.001	0.76
Intercept	AEB: Parcel 4 (BL)		ia4	0.42	0.09	4.51	< 0.001	0.69
Intercept	AEB: Parcel 5 (BL)		ia5	0.32	0.09	3.68	< 0.001	0.57
Intercept	AEB: Parcel 6 (BL)		ia6	0.89	0.15	5.77	< 0.001	0.93
Intercept	ASO: Parcel 1 (BL)		ia7	0.92	0.17	5.53	< 0.001	0.99
Intercept	ASO: Parcel 2 (BL)		ia8	0.84	0.16	5.36	< 0.001	0.98
Intercept	ASO: Parcel 3 (BL)		ia9	0.69	0.15	4.51	< 0.001	0.8
Intercept	ASO: Parcel 4 (BL)		ia10	0.62	0.14	4.31	< 0.001	0.72
Intercept	ASO: Parcel 5 (BL)		ia11	1.01	0.16	6.36	< 0.001	1.14
Intercept	ASO: Parcel 6 (BL)		ia12	1.31	0.24	5.56	< 0.001	1.1
Intercept	AEB: Parcel 1 (FU)		ia1	1.04	0.13	7.83	< 0.001	1.23
Intercept	AEB: Parcel 2 (FU)		ia2	0.77	0.15	5.21	< 0.001	0.97
Intercept	AEB: Parcel 3 (FU)		ia3	0.53	0.11	4.6	< 0.001	0.8

Table B.6 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Intercept	AEB: Parcel 4 (FU)		ia4	0.42	0.09	4.51	< 0.001	0.72
Intercept	AEB: Parcel 5 (FU)		ia5	0.32	0.09	3.68	< 0.001	0.6
Intercept	AEB: Parcel 6 (FU)		ia6	0.89	0.15	5.77	< 0.001	0.98
Intercept	ASO: Parcel 1 (FU)		ia7	0.92	0.17	5.53	< 0.001	0.97
Intercept	ASO: Parcel 2 (FU)		ia8	0.84	0.16	5.36	< 0.001	0.96
Intercept	ASO: Parcel 3 (FU)		ia9	0.69	0.15	4.51	< 0.001	0.79
Intercept	ASO: Parcel 4 (FU)		ia10	0.62	0.14	4.31	< 0.001	0.72
Intercept	ASO: Parcel 5 (FU)		ia11	1.01	0.16	6.36	< 0.001	1.12
Intercept	ASO: Parcel 6 (FU)		ia12	1.31	0.24	5.56	< 0.001	1.08
Intercept	Male			0.47	0	NA	NA	0.93
Intercept	Socioeconomic deprivation (IMD)			-0.01	0	NA	NA	-0.01
Intercept	Cannabis Use at baseline			0.12	0	NA	NA	0.38
Intercept	Age (years)			19.08	0	NA	NA	6.35
Intercept	Non-white ethnicity			0.23	0	NA	NA	0.54
Intercept	Any family psychiatric history			0.11	0	NA	NA	0.35
Intercept	Urban/rural index			5.47	0	NA	NA	7.31
Intercept	Mother's educational qualifications			1.73	0	NA	NA	1.56
Intercept	ASO (BL)			0	0	NA	NA	0
Intercept	ASO (FU)			0	0	NA	NA	0
Intercept	AEB (BL)			0	0	NA	NA	0
Intercept	AEB (FU)			0	0	NA	NA	0
Covariate regression	ASO (BL)	Male		0.1	0.03	3.12	0.002	0.07
Covariate regression	ASO (BL)	Socioeconomic deprivation (IMD)		-0.04	0.02	-2.45	0.014	-0.06

Table B.6 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	ASO (BL)	Cannabis Use at baseline		0.05	0.05	0.97	0.333	0.02
Covariate regression	ASO (BL)	Age (years)		0	0	0.15	0.881	0
Covariate regression	ASO (BL)	Non-white ethnicity		0.11	0.04	2.75	0.006	0.07
Covariate regression	ASO (BL)	Any family psychiatric history		0.16	0.05	2.87	0.004	0.07
Covariate regression	ASO (BL)	Urban/rural index		-0.01	0.02	-0.33	0.741	-0.01
Covariate regression	ASO (BL)	Mother's educational qualifications		-0.06	0.01	-4.3	< 0.001	-0.09
Covariate regression	AEB (BL)	Male		-0.03	0.03	-1.11	0.268	-0.02
Covariate regression	AEB (BL)	Socioeconomic deprivation (IMD)		-0.05	0.02	-3.12	0.002	-0.08
Covariate regression	AEB (BL)	Cannabis Use at baseline		0.12	0.04	3.02	0.003	0.07
Covariate regression	AEB (BL)	Age (years)		-0.01	0	-3.26	0.001	-0.07
Covariate regression	AEB (BL)	Non-white ethnicity		0.12	0.04	3.25	0.001	0.09
Covariate regression	AEB (BL)	Any family psychiatric history		0.13	0.04	2.84	0.004	0.07
Covariate regression	AEB (BL)	Urban/rural index		0.04	0.02	2.04	0.041	0.05
Covariate regression	AEB (BL)	Mother's educational qualifications		-0.06	0.01	-5.25	< 0.001	-0.12
Covariate regression	ASO (FU)	Male		-0.01	0.02	-0.45	0.652	-0.01
Covariate regression	ASO (FU)	Socioeconomic deprivation (IMD)		0.01	0.01	0.91	0.36	0.02
Covariate regression	ASO (FU)	Cannabis Use at baseline		0.06	0.04	1.4	0.161	0.03
Covariate regression	ASO (FU)	Age (years)		0	0	-0.29	0.768	0

Table B.6 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	ASO (FU)	Non-white ethnicity		0.01	0.03	0.4	0.688	0.01
Covariate regression	ASO (FU)	Any family psychiatric history		0.01	0.04	0.24	0.812	0
Covariate regression	ASO (FU)	Urban/rural index		0	0.01	-0.2	0.844	0
Covariate regression	ASO (FU)	Mother's educational qualifications		-0.03	0.01	-2.3	0.021	-0.04
Covariate regression	AEB (FU)	Male		-0.04	0.02	-2.09	0.037	-0.04
Covariate regression	AEB (FU)	Socioeconomic deprivation (IMD)		0.01	0.01	0.98	0.33	0.02
Covariate regression	AEB (FU)	Cannabis Use at baseline		0.14	0.04	3.48	< 0.001	0.09
Covariate regression	AEB (FU)	Age (years)		0	0	-1.09	0.274	-0.02
Covariate regression	AEB (FU)	Non-white ethnicity		-0.04	0.03	-1.56	0.119	-0.04
Covariate regression	AEB (FU)	Any family psychiatric history		0.05	0.04	1.25	0.211	0.03
Covariate regression	AEB (FU)	Urban/rural index		-0.01	0.01	-1.23	0.219	-0.02
Covariate regression	AEB (FU)	Mother's educational qualifications		-0.03	0.01	-3.07	0.002	-0.06
Covariance	ASO (BL)	AEB (BL)		0.14	0.01	13.23	< 0.001	0.37
Covariance	ASO (FU)	AEB (FU)		0.06	0.01	9.64	< 0.001	0.45
Covariance	AEB: Parcel 1 (BL)	AEB: Parcel 1 (FU)		0.11	0.02	6.87	< 0.001	0.23
Covariance	AEB: Parcel 2 (BL)	AEB: Parcel 2 (FU)		0.06	0.01	5.24	< 0.001	0.2
Covariance	AEB: Parcel 3 (BL)	AEB: Parcel 3 (FU)		0.08	0.01	8.1	< 0.001	0.34
Covariance	AEB: Parcel 4 (BL)	AEB: Parcel 4 (FU)		0.04	0.01	4.61	< 0.001	0.18
Covariance	AEB: Parcel 5 (BL)	AEB: Parcel 5 (FU)		0.06	0.01	6.63	< 0.001	0.33
Covariance	AEB: Parcel 6 (BL)	AEB: Parcel 6 (FU)		0.2	0.02	11.47	< 0.001	0.43

Table B.6 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariance	ASO: Parcel 1 (BL)	ASO: Parcel 1 (FU)		0.11	0.01	8.58	< 0.001	0.28
Covariance	ASO: Parcel 2 (BL)	ASO: Parcel 2 (FU)		0.09	0.01	9.02	< 0.001	0.3
Covariance	ASO: Parcel 3 (BL)	ASO: Parcel 3 (FU)		0.11	0.01	9.42	< 0.001	0.32
Covariance	ASO: Parcel 4 (BL)	ASO: Parcel 4 (FU)		0.13	0.01	10.24	< 0.001	0.36
Covariance	ASO: Parcel 5 (BL)	ASO: Parcel 5 (FU)		0.1	0.01	8.99	< 0.001	0.29
Covariance	ASO: Parcel 6 (BL)	ASO: Parcel 6 (FU)		0.06	0.02	3.77	< 0.001	0.14

Table B.6: Parameter estimates of the cross-lagged model of ASO and AEB fit to NSPN data with a robust maximum-likelihood estimator, with missing data estimated using full-information maximum likelihood. Parameters with the same Equality constraint label were fixed to be equal. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate.

Table B.7: Parameter estimates from cross-lagged models of Asociality and Paranoid Ideation

Parameter type	Factor or threshold	Item or factor	Equality constraint	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	ASO (BL)	ASO: Parcel 1 (BL)	l7	1	0	NA	NA	0.74
Loading	ASO (BL)	ASO: Parcel 2 (BL)	l8	0.94	0.02	46.06	< 0.001	0.76
Loading	ASO (BL)	ASO: Parcel 3 (BL)	l9	0.93	0.02	39.61	< 0.001	0.74
Loading	ASO (BL)	ASO: Parcel 4 (BL)	l10	0.86	0.02	38.48	< 0.001	0.71
Loading	ASO (BL)	ASO: Parcel 5 (BL)	l11	0.96	0.02	47.15	< 0.001	0.75
Loading	ASO (BL)	ASO: Parcel 6 (BL)	l12	1.43	0.03	46.89	< 0.001	0.83
Loading	ASO (FU)	ASO: Parcel 1 (FU)	l7	1	0	NA	NA	0.75
Loading	ASO (FU)	ASO: Parcel 2 (FU)	l8	0.94	0.02	46.06	< 0.001	0.76
Loading	ASO (FU)	ASO: Parcel 3 (FU)	l9	0.93	0.02	39.61	< 0.001	0.75
Loading	ASO (FU)	ASO: Parcel 4 (FU)	l10	0.86	0.02	38.48	< 0.001	0.71
Loading	ASO (FU)	ASO: Parcel 5 (FU)	l11	0.96	0.02	47.15	< 0.001	0.76

Table B.7 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	ASO (FU)	ASO: Parcel 6 (FU)	l12	1.43	0.03	46.89	< 0.001	0.84
Loading	PI (BL)	PI: Parcel 1 (BL)	l13	1	0	NA	NA	0.77
Loading	PI (BL)	PI: Parcel 2 (BL)	l14	0.96	0.02	46.9	< 0.001	0.74
Loading	PI (BL)	PI: Parcel 3 (BL)	l15	0.86	0.02	48.2	< 0.001	0.78
Loading	PI (BL)	PI: Parcel 4 (BL)	l16	1.41	0.03	52.98	< 0.001	0.87
Loading	PI (FU)	PI: Parcel 1 (FU)	l13	1	0	NA	NA	0.77
Loading	PI (FU)	PI: Parcel 2 (FU)	l14	0.96	0.02	46.9	< 0.001	0.74
Loading	PI (FU)	PI: Parcel 3 (FU)	l15	0.86	0.02	48.2	< 0.001	0.78
Loading	PI (FU)	PI: Parcel 4 (FU)	l16	1.41	0.03	52.98	< 0.001	0.87
Regression	ASO (FU)	ASO (BL)		0.84	0.03	32.2	< 0.001	0.82
Regression	ASO (FU)	PI (BL)		-0.01	0.02	-0.51	0.608	-0.01
Regression	PI (FU)	PI (BL)		0.64	0.03	19.76	< 0.001	0.64
Regression	PI (FU)	ASO (BL)		0.1	0.03	2.92	0.004	0.09
Intercept	ASO: Parcel 1 (BL)		ia7	0.93	0.17	5.62	< 0.001	1
Intercept	ASO: Parcel 2 (BL)		ia8	0.85	0.16	5.46	< 0.001	0.99
Intercept	ASO: Parcel 3 (BL)		ia9	0.7	0.15	4.55	< 0.001	0.81
Intercept	ASO: Parcel 4 (BL)		ia10	0.63	0.14	4.36	< 0.001	0.74
Intercept	ASO: Parcel 5 (BL)		ia11	1.02	0.16	6.39	< 0.001	1.15
Intercept	ASO: Parcel 6 (BL)		ia12	1.33	0.24	5.6	< 0.001	1.11
Intercept	PI: Parcel 1 (BL)		ia13	1.63	0.18	8.84	< 0.001	1.59
Intercept	PI: Parcel 2 (BL)		ia14	1.58	0.18	9	< 0.001	1.55
Intercept	PI: Parcel 3 (BL)		ia15	1.25	0.16	7.92	< 0.001	1.44
Intercept	PI: Parcel 4 (BL)		ia16	1.99	0.26	7.76	< 0.001	1.57
Intercept	ASO: Parcel 1 (FU)		ia7	0.93	0.17	5.62	< 0.001	0.99

Table B.7 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Intercept	ASO: Parcel 2 (FU)		ia8	0.85	0.16	5.46	< 0.001	0.98
Intercept	ASO: Parcel 3 (FU)		ia9	0.7	0.15	4.55	< 0.001	0.8
Intercept	ASO: Parcel 4 (FU)		ia10	0.63	0.14	4.36	< 0.001	0.73
Intercept	ASO: Parcel 5 (FU)		ia11	1.02	0.16	6.39	< 0.001	1.13
Intercept	ASO: Parcel 6 (FU)		ia12	1.33	0.24	5.6	< 0.001	1.09
Intercept	PI: Parcel 1 (FU)		ia13	1.63	0.18	8.84	< 0.001	1.6
Intercept	PI: Parcel 2 (FU)		ia14	1.58	0.18	9	< 0.001	1.55
Intercept	PI: Parcel 3 (FU)		ia15	1.25	0.16	7.92	< 0.001	1.45
Intercept	PI: Parcel 4 (FU)		ia16	1.99	0.26	7.76	< 0.001	1.57
Intercept	Male			0.47	0	NA	NA	0.93
Intercept	Socioeconomic deprivation (IMD)			-0.01	0	NA	NA	-0.01
Intercept	Cannabis Use at baseline			0.12	0	NA	NA	0.38
Intercept	Age (years)			19.08	0	NA	NA	6.35
Intercept	Non-white ethnicity			0.23	0	NA	NA	0.54
Intercept	Any family psychiatric history			0.11	0	NA	NA	0.35
Intercept	Urban/rural index			5.47	0	NA	NA	7.31
Intercept	Mother's educational qualifications			1.73	0	NA	NA	1.56
Intercept	ASO (BL)			0	0	NA	NA	0
Intercept	ASO (FU)			0	0	NA	NA	0
Intercept	PI (BL)			0	0	NA	NA	0
Intercept	PI (FU)			0	0	NA	NA	0
Covariate regression	ASO (BL)	Male		0.09	0.03	3.11	0.002	0.07
Covariate regression	ASO (BL)	Socioeconomic deprivation (IMD)		-0.04	0.02	-2.42	0.015	-0.06

Table B.7 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	ASO (BL)	Cannabis Use at baseline		0.05	0.05	0.98	0.325	0.02
Covariate regression	ASO (BL)	Age (years)		0	0	0.13	0.898	0
Covariate regression	ASO (BL)	Non-white ethnicity		0.11	0.04	2.74	0.006	0.07
Covariate regression	ASO (BL)	Any family psychiatric history		0.15	0.05	2.86	0.004	0.07
Covariate regression	ASO (BL)	Urban/rural index		-0.01	0.02	-0.4	0.689	-0.01
Covariate regression	ASO (BL)	Mother's educational qualifications		-0.06	0.01	-4.32	< 0.001	-0.09
Covariate regression	PI (BL)	Male		-0.09	0.03	-2.5	0.012	-0.05
Covariate regression	PI (BL)	Socioeconomic deprivation (IMD)		-0.05	0.02	-2.47	0.013	-0.06
Covariate regression	PI (BL)	Cannabis Use at baseline		0.12	0.05	2.29	0.022	0.05
Covariate regression	PI (BL)	Age (years)		-0.03	0.01	-5.3	< 0.001	-0.11
Covariate regression	PI (BL)	Non-white ethnicity		0.07	0.04	1.6	0.11	0.04
Covariate regression	PI (BL)	Any family psychiatric history		0.24	0.06	4.01	< 0.001	0.09
Covariate regression	PI (BL)	Urban/rural index		0.03	0.02	1.19	0.234	0.03
Covariate regression	PI (BL)	Mother's educational qualifications		-0.09	0.02	-5.69	< 0.001	-0.12
Covariate regression	ASO (FU)	Male		-0.01	0.02	-0.4	0.693	-0.01
Covariate regression	ASO (FU)	Socioeconomic deprivation (IMD)		0.02	0.01	1.1	0.27	0.02
Covariate regression	ASO (FU)	Cannabis Use at baseline		0.06	0.04	1.36	0.174	0.03
Covariate regression	ASO (FU)	Age (years)		0	0	-0.24	0.81	0

Table B.7 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	ASO (FU)	Non-white ethnicity		0.01	0.03	0.33	0.74	0.01
Covariate regression	ASO (FU)	Any family psychiatric history		0.01	0.04	0.16	0.877	0
Covariate regression	ASO (FU)	Urban/rural index		0	0.01	-0.34	0.731	0
Covariate regression	ASO (FU)	Mother's educational qualifications		-0.02	0.01	-2.18	0.029	-0.04
Covariate regression	PI (FU)	Male		-0.05	0.03	-1.58	0.114	-0.03
Covariate regression	PI (FU)	Socioeconomic deprivation (IMD)		0.05	0.02	2.65	0.008	0.06
Covariate regression	PI (FU)	Cannabis Use at baseline		0.1	0.05	1.87	0.062	0.04
Covariate regression	PI (FU)	Age (years)		-0.01	0	-1.48	0.138	-0.02
Covariate regression	PI (FU)	Non-white ethnicity		0.01	0.04	0.16	0.875	0
Covariate regression	PI (FU)	Any family psychiatric history		0.05	0.05	0.87	0.385	0.02
Covariate regression	PI (FU)	Urban/rural index		-0.03	0.02	-2.16	0.031	-0.03
Covariate regression	PI (FU)	Mother's educational qualifications		-0.04	0.01	-2.67	0.007	-0.05
Covariance	ASO (BL)	PI (BL)		0.31	0.01	21.97	< 0.001	0.59
Covariance	ASO (FU)	PI (FU)		0.14	0.01	13.99	< 0.001	0.6
Covariance	ASO: Parcel 1 (BL)	ASO: Parcel 1 (FU)		0.11	0.01	8.52	< 0.001	0.27
Covariance	ASO: Parcel 2 (BL)	ASO: Parcel 2 (FU)		0.1	0.01	9.18	< 0.001	0.3
Covariance	ASO: Parcel 3 (BL)	ASO: Parcel 3 (FU)		0.11	0.01	9.42	< 0.001	0.32
Covariance	ASO: Parcel 4 (BL)	ASO: Parcel 4 (FU)		0.13	0.01	10.31	< 0.001	0.36
Covariance	ASO: Parcel 5 (BL)	ASO: Parcel 5 (FU)		0.1	0.01	9.09	< 0.001	0.29
Covariance	ASO: Parcel 6 (BL)	ASO: Parcel 6 (FU)		0.06	0.02	3.83	< 0.001	0.14

Table B.7 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariance	PI: Parcel 1 (BL)	PI: Parcel 1 (FU)		0.11	0.02	7.55	< 0.001	0.27
Covariance	PI: Parcel 2 (BL)	PI: Parcel 2 (FU)		0.15	0.02	9.86	< 0.001	0.32
Covariance	PI: Parcel 3 (BL)	PI: Parcel 3 (FU)		0.06	0.01	5.23	< 0.001	0.19
Covariance	PI: Parcel 4 (BL)	PI: Parcel 4 (FU)		0.06	0.02	3.2	0.001	0.14

Table B.7: Parameter estimates of the cross-lagged model of ASO and PI fit to NSPN data with a robust maximum-likelihood estimator, with missing data estimated using full-information maximum likelihood. Parameters with the same Equality constraint label were fixed to be equal. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate.

Table B.8: Parameter estimates from cross-lagged models of Anomalous Experiences & Beliefs and Paranoid Ideation

Parameter type	Factor or threshold	Item or factor	Equality constraint	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	PI (BL)	PI: Parcel 1 (BL)	l13	1	0	NA	NA	0.77
Loading	PI (BL)	PI: Parcel 2 (BL)	l14	0.94	0.02	46.69	< 0.001	0.73
Loading	PI (BL)	PI: Parcel 3 (BL)	l15	0.86	0.02	47.62	< 0.001	0.78
Loading	PI (BL)	PI: Parcel 4 (BL)	l16	1.41	0.03	52.65	< 0.001	0.87
Loading	PI (FU)	PI: Parcel 1 (FU)	l13	1	0	NA	NA	0.77
Loading	PI (FU)	PI: Parcel 2 (FU)	l14	0.94	0.02	46.69	< 0.001	0.73
Loading	PI (FU)	PI: Parcel 3 (FU)	l15	0.86	0.02	47.62	< 0.001	0.78
Loading	PI (FU)	PI: Parcel 4 (FU)	l16	1.41	0.03	52.65	< 0.001	0.87
Loading	AEB (BL)	AEB: Parcel 1 (BL)	l1	1	0	NA	NA	0.65
Loading	AEB (BL)	AEB: Parcel 2 (BL)	l2	1.1	0.03	32.7	< 0.001	0.75
Loading	AEB (BL)	AEB: Parcel 3 (BL)	l3	0.83	0.03	26.31	< 0.001	0.69
Loading	AEB (BL)	AEB: Parcel 4 (BL)	l4	0.69	0.03	22.91	< 0.001	0.65

Table B.8 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	AEB (BL)	AEB: Parcel 5 (BL)	l5	0.63	0.03	20.79	< 0.001	0.65
Loading	AEB (BL)	AEB: Parcel 6 (BL)	l6	1.16	0.04	29.98	< 0.001	0.7
Loading	AEB (FU)	AEB: Parcel 1 (FU)	l1	1	0	NA	NA	0.61
Loading	AEB (FU)	AEB: Parcel 2 (FU)	l2	1.1	0.03	32.7	< 0.001	0.72
Loading	AEB (FU)	AEB: Parcel 3 (FU)	l3	0.83	0.03	26.31	< 0.001	0.65
Loading	AEB (FU)	AEB: Parcel 4 (FU)	l4	0.69	0.03	22.91	< 0.001	0.61
Loading	AEB (FU)	AEB: Parcel 5 (FU)	l5	0.63	0.03	20.79	< 0.001	0.6
Loading	AEB (FU)	AEB: Parcel 6 (FU)	l6	1.16	0.04	29.98	< 0.001	0.66
Regression	PI (FU)	PI (BL)		0.65	0.03	18.82	< 0.001	0.65
Regression	PI (FU)	AEB (BL)		0.1	0.05	2	0.045	0.07
Regression	AEB (FU)	AEB (BL)		0.61	0.04	14.87	< 0.001	0.68
Regression	AEB (FU)	PI (BL)		0.04	0.02	1.84	0.066	0.07
Intercept	AEB: Parcel 1 (BL)		ia1	1.07	0.13	7.98	< 0.001	1.21
Intercept	AEB: Parcel 2 (BL)		ia2	0.81	0.15	5.43	< 0.001	0.96
Intercept	AEB: Parcel 3 (BL)		ia3	0.55	0.11	4.9	< 0.001	0.79
Intercept	AEB: Parcel 4 (BL)		ia4	0.44	0.09	4.74	< 0.001	0.72
Intercept	AEB: Parcel 5 (BL)		ia5	0.34	0.09	3.95	< 0.001	0.6
Intercept	AEB: Parcel 6 (BL)		ia6	0.93	0.16	5.89	< 0.001	0.98
Intercept	PI: Parcel 1 (BL)		ia13	1.62	0.18	8.78	< 0.001	1.59
Intercept	PI: Parcel 2 (BL)		ia14	1.56	0.17	9.01	< 0.001	1.54
Intercept	PI: Parcel 3 (BL)		ia15	1.24	0.16	7.84	< 0.001	1.44
Intercept	PI: Parcel 4 (BL)		ia16	1.98	0.26	7.7	< 0.001	1.56
Intercept	AEB: Parcel 1 (FU)		ia1	1.07	0.13	7.98	< 0.001	1.26
Intercept	AEB: Parcel 2 (FU)		ia2	0.81	0.15	5.43	< 0.001	1.01

Table B.8 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Intercept	AEB: Parcel 3 (FU)		ia3	0.55	0.11	4.9	< 0.001	0.83
Intercept	AEB: Parcel 4 (FU)		ia4	0.44	0.09	4.74	< 0.001	0.76
Intercept	AEB: Parcel 5 (FU)		ia5	0.34	0.09	3.95	< 0.001	0.63
Intercept	AEB: Parcel 6 (FU)		ia6	0.93	0.16	5.89	< 0.001	1.03
Intercept	PI: Parcel 1 (FU)		ia13	1.62	0.18	8.78	< 0.001	1.59
Intercept	PI: Parcel 2 (FU)		ia14	1.56	0.17	9.01	< 0.001	1.54
Intercept	PI: Parcel 3 (FU)		ia15	1.24	0.16	7.84	< 0.001	1.44
Intercept	PI: Parcel 4 (FU)		ia16	1.98	0.26	7.7	< 0.001	1.57
Intercept	Male			0.47	0	NA	NA	0.93
Intercept	Socioeconomic deprivation (IMD)			-0.01	0	NA	NA	-0.01
Intercept	Cannabis Use at baseline			0.12	0	NA	NA	0.38
Intercept	Age (years)			19.08	0	NA	NA	6.35
Intercept	Non-white ethnicity			0.23	0	NA	NA	0.54
Intercept	Any family psychiatric history			0.11	0	NA	NA	0.35
Intercept	Urban/rural index			5.47	0	NA	NA	7.31
Intercept	Mother's educational qualifications			1.73	0	NA	NA	1.56
Intercept	PI (BL)			0	0	NA	NA	0
Intercept	PI (FU)			0	0	NA	NA	0
Intercept	AEB (BL)			0	0	NA	NA	0
Intercept	AEB (FU)			0	0	NA	NA	0
Covariate regression	PI (BL)	Male		-0.09	0.03	-2.51	0.012	-0.05
Covariate regression	PI (BL)	Socioeconomic deprivation (IMD)		-0.05	0.02	-2.49	0.013	-0.06

Table B.8 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	PI (BL)	Cannabis Use at baseline		0.12	0.05	2.28	0.022	0.05
Covariate regression	PI (BL)	Age (years)		-0.03	0.01	-5.29	< 0.001	-0.11
Covariate regression	PI (BL)	Non-white ethnicity		0.07	0.04	1.6	0.11	0.04
Covariate regression	PI (BL)	Any family psychiatric history		0.24	0.06	4	< 0.001	0.09
Covariate regression	PI (BL)	Urban/rural index		0.03	0.02	1.22	0.221	0.03
Covariate regression	PI (BL)	Mother's educational qualifications		-0.09	0.02	-5.66	< 0.001	-0.12
Covariate regression	AEB (BL)	Male		-0.03	0.03	-1.05	0.292	-0.02
Covariate regression	AEB (BL)	Socioeconomic deprivation (IMD)		-0.05	0.02	-3.09	0.002	-0.08
Covariate regression	AEB (BL)	Cannabis Use at baseline		0.12	0.04	3.01	0.003	0.07
Covariate regression	AEB (BL)	Age (years)		-0.01	0	-3.48	0.001	-0.07
Covariate regression	AEB (BL)	Non-white ethnicity		0.12	0.04	3.25	0.001	0.09
Covariate regression	AEB (BL)	Any family psychiatric history		0.13	0.04	2.88	0.004	0.07
Covariate regression	AEB (BL)	Urban/rural index		0.04	0.02	1.91	0.056	0.05
Covariate regression	AEB (BL)	Mother's educational qualifications		-0.06	0.01	-5.27	< 0.001	-0.12
Covariate regression	PI (FU)	Male		-0.05	0.03	-1.43	0.152	-0.03
Covariate regression	PI (FU)	Socioeconomic deprivation (IMD)		0.04	0.02	2.6	0.009	0.06
Covariate regression	PI (FU)	Cannabis Use at baseline		0.08	0.05	1.58	0.115	0.04
Covariate regression	PI (FU)	Age (years)		0	0	-1.22	0.223	-0.02

Table B.8 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	PI (FU)	Non-white ethnicity		0.01	0.04	0.22	0.824	0
Covariate regression	PI (FU)	Any family psychiatric history		0.04	0.05	0.76	0.446	0.02
Covariate regression	PI (FU)	Urban/rural index		-0.03	0.02	-2.25	0.024	-0.03
Covariate regression	PI (FU)	Mother's educational qualifications		-0.04	0.01	-2.74	0.006	-0.06
Covariate regression	AEB (FU)	Male		-0.04	0.02	-1.82	0.069	-0.04
Covariate regression	AEB (FU)	Socioeconomic deprivation (IMD)		0.01	0.01	0.99	0.325	0.02
Covariate regression	AEB (FU)	Cannabis Use at baseline		0.14	0.04	3.53	< 0.001	0.09
Covariate regression	AEB (FU)	Age (years)		0	0	-0.77	0.439	-0.01
Covariate regression	AEB (FU)	Non-white ethnicity		-0.04	0.03	-1.4	0.162	-0.03
Covariate regression	AEB (FU)	Any family psychiatric history		0.04	0.04	1.12	0.264	0.03
Covariate regression	AEB (FU)	Urban/rural index		-0.01	0.01	-1.43	0.153	-0.02
Covariate regression	AEB (FU)	Mother's educational qualifications		-0.03	0.01	-3.11	0.002	-0.06
Covariance	PI (BL)	AEB (BL)		0.27	0.01	19.56	< 0.001	0.62
Covariance	PI (FU)	AEB (FU)		0.12	0.01	12.58	< 0.001	0.63
Covariance	AEB: Parcel 1 (BL)	AEB: Parcel 1 (FU)		0.1	0.02	6.68	< 0.001	0.22
Covariance	AEB: Parcel 2 (BL)	AEB: Parcel 2 (FU)		0.06	0.01	5.37	< 0.001	0.21
Covariance	AEB: Parcel 3 (BL)	AEB: Parcel 3 (FU)		0.09	0.01	8.51	< 0.001	0.35
Covariance	AEB: Parcel 4 (BL)	AEB: Parcel 4 (FU)		0.04	0.01	4.55	< 0.001	0.17
Covariance	AEB: Parcel 5 (BL)	AEB: Parcel 5 (FU)		0.06	0.01	6.85	< 0.001	0.34
Covariance	AEB: Parcel 6 (BL)	AEB: Parcel 6 (FU)		0.19	0.02	11.28	< 0.001	0.42

Table B.8 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariance	PI: Parcel 1 (BL)	PI: Parcel 1 (FU)		0.11	0.02	7.26	< 0.001	0.26
Covariance	PI: Parcel 2 (BL)	PI: Parcel 2 (FU)		0.15	0.02	9.99	< 0.001	0.32
Covariance	PI: Parcel 3 (BL)	PI: Parcel 3 (FU)		0.06	0.01	5.17	< 0.001	0.19
Covariance	PI: Parcel 4 (BL)	PI: Parcel 4 (FU)		0.05	0.02	3.13	0.002	0.14

Table B.8: Parameter estimates of the cross-lagged model of AEB and PI fit to NSPN data with a robust maximum-likelihood estimator, with missing data estimated using full-information maximum likelihood. Parameters with the same Equality constraint label were fixed to be equal. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate.

Table B.9: Parameter estimates from cross-lagged mediation models of Asociality, Anomalous Experiences & Beliefs and social support

Parameter type	Factor or threshold	Item or factor	Equality constraint	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	ASO (BL)	ASO: Parcel 1 (BL)	l7	1	0	NA	NA	0.75
Loading	ASO (BL)	ASO: Parcel 2 (BL)	l8	0.93	0.02	46.14	< 0.001	0.76
Loading	ASO (BL)	ASO: Parcel 3 (BL)	l9	0.93	0.02	39.63	< 0.001	0.74
Loading	ASO (BL)	ASO: Parcel 4 (BL)	l10	0.85	0.02	38.01	< 0.001	0.7
Loading	ASO (BL)	ASO: Parcel 5 (BL)	l11	0.96	0.02	47.04	< 0.001	0.75
Loading	ASO (BL)	ASO: Parcel 6 (BL)	l12	1.41	0.03	46.84	< 0.001	0.83
Loading	ASO (FU)	ASO: Parcel 1 (FU)	l7	1	0	NA	NA	0.75
Loading	ASO (FU)	ASO: Parcel 2 (FU)	l8	0.93	0.02	46.14	< 0.001	0.77
Loading	ASO (FU)	ASO: Parcel 3 (FU)	l9	0.93	0.02	39.63	< 0.001	0.75
Loading	ASO (FU)	ASO: Parcel 4 (FU)	l10	0.85	0.02	38.01	< 0.001	0.71
Loading	ASO (FU)	ASO: Parcel 5 (FU)	l11	0.96	0.02	47.04	< 0.001	0.76
Loading	ASO (FU)	ASO: Parcel 6 (FU)	l12	1.41	0.03	46.84	< 0.001	0.83

Table B.9 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	AEB (BL)	AEB: Parcel 1 (BL)	l1	1	0	NA	NA	0.64
Loading	AEB (BL)	AEB: Parcel 2 (BL)	l2	1.11	0.03	32.06	< 0.001	0.75
Loading	AEB (BL)	AEB: Parcel 3 (BL)	l3	0.86	0.03	26.18	< 0.001	0.7
Loading	AEB (BL)	AEB: Parcel 4 (BL)	l4	0.69	0.03	22.57	< 0.001	0.65
Loading	AEB (BL)	AEB: Parcel 5 (BL)	l5	0.65	0.03	20.67	< 0.001	0.66
Loading	AEB (BL)	AEB: Parcel 6 (BL)	l6	1.15	0.04	29.32	< 0.001	0.69
Loading	AEB (FU)	AEB: Parcel 1 (FU)	l1	1	0	NA	NA	0.6
Loading	AEB (FU)	AEB: Parcel 2 (FU)	l2	1.11	0.03	32.06	< 0.001	0.71
Loading	AEB (FU)	AEB: Parcel 3 (FU)	l3	0.86	0.03	26.18	< 0.001	0.66
Loading	AEB (FU)	AEB: Parcel 4 (FU)	l4	0.69	0.03	22.57	< 0.001	0.61
Loading	AEB (FU)	AEB: Parcel 5 (FU)	l5	0.65	0.03	20.67	< 0.001	0.62
Loading	AEB (FU)	AEB: Parcel 6 (FU)	l6	1.15	0.04	29.32	< 0.001	0.65
Regression	ASO (FU)	ASO (BL)		0.68	0.02	28.21	< 0.001	0.66
Regression	ASO (FU)	AEB (BL)		-0.04	0.03	-1.52	0.128	-0.03
Regression	AEB (FU)	AEB (BL)		0.63	0.03	18.95	< 0.001	0.7
Regression	AEB (FU)	ASO (BL)		-0.03	0.02	-1.25	0.212	-0.04
Regression	ASO (FU)	Family Relationship Quality		-0.09	0.01	-6.87	< 0.001	-0.12
Regression	ASO (FU)	Friendship Quality		-0.18	0.01	-12.48	< 0.001	-0.25
Regression	AEB (FU)	Family Relationship Quality		-0.05	0.01	-4.08	< 0.001	-0.1
Regression	AEB (FU)	Friendship Quality		-0.06	0.01	-4.59	< 0.001	-0.11
Regression	Family Relationship Quality	ASO (BL)		-0.49	0.04	-12.45	< 0.001	-0.34
Regression	Family Relationship Quality	AEB (BL)		-0.05	0.06	-0.95	0.341	-0.03
Regression	Friendship Quality	ASO (BL)		-0.67	0.04	-17.25	< 0.001	-0.47

Table B.9 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Regression	Friendship Quality	AEB (BL)		0.03	0.05	0.5	0.617	0.02
Intercept	AEB: Parcel 1 (BL)		ia1	1.04	0.13	7.93	< 0.001	1.18
Intercept	AEB: Parcel 2 (BL)		ia2	0.78	0.15	5.29	< 0.001	0.92
Intercept	AEB: Parcel 3 (BL)		ia3	0.53	0.11	4.67	< 0.001	0.76
Intercept	AEB: Parcel 4 (BL)		ia4	0.42	0.09	4.58	< 0.001	0.69
Intercept	AEB: Parcel 5 (BL)		ia5	0.32	0.09	3.74	< 0.001	0.57
Intercept	AEB: Parcel 6 (BL)		ia6	0.89	0.15	5.85	< 0.001	0.94
Intercept	ASO: Parcel 1 (BL)		ia7	0.94	0.16	6.06	< 0.001	1
Intercept	ASO: Parcel 2 (BL)		ia8	0.85	0.14	5.89	< 0.001	0.99
Intercept	ASO: Parcel 3 (BL)		ia9	0.71	0.14	4.92	< 0.001	0.81
Intercept	ASO: Parcel 4 (BL)		ia10	0.63	0.13	4.77	< 0.001	0.74
Intercept	ASO: Parcel 5 (BL)		ia11	1.03	0.15	6.93	< 0.001	1.16
Intercept	ASO: Parcel 6 (BL)		ia12	1.33	0.22	6.1	< 0.001	1.12
Intercept	AEB: Parcel 1 (FU)		ia1	1.04	0.13	7.93	< 0.001	1.23
Intercept	AEB: Parcel 2 (FU)		ia2	0.78	0.15	5.29	< 0.001	0.98
Intercept	AEB: Parcel 3 (FU)		ia3	0.53	0.11	4.67	< 0.001	0.8
Intercept	AEB: Parcel 4 (FU)		ia4	0.42	0.09	4.58	< 0.001	0.72
Intercept	AEB: Parcel 5 (FU)		ia5	0.32	0.09	3.74	< 0.001	0.6
Intercept	AEB: Parcel 6 (FU)		ia6	0.89	0.15	5.85	< 0.001	0.98
Intercept	ASO: Parcel 1 (FU)		ia7	0.94	0.16	6.06	< 0.001	0.99
Intercept	ASO: Parcel 2 (FU)		ia8	0.85	0.14	5.89	< 0.001	0.98
Intercept	ASO: Parcel 3 (FU)		ia9	0.71	0.14	4.92	< 0.001	0.8
Intercept	ASO: Parcel 4 (FU)		ia10	0.63	0.13	4.77	< 0.001	0.73

Table B.9 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Intercept	ASO: Parcel 5 (FU)		ia11	1.03	0.15	6.93	< 0.001	1.14
Intercept	ASO: Parcel 6 (FU)		ia12	1.33	0.22	6.1	< 0.001	1.1
Intercept	Family Relationship Quality			-0.27	0.27	-0.99	0.32	-0.27
Intercept	Friendship Quality			0.64	0.28	2.3	0.022	0.64
Intercept	Male			0.47	0	NA	NA	0.93
Intercept	Socioeconomic deprivation (IMD)			-0.01	0	NA	NA	-0.01
Intercept	Cannabis Use at baseline			0.12	0	NA	NA	0.38
Intercept	Age (years)			19.08	0	NA	NA	6.35
Intercept	Non-white ethnicity			0.23	0	NA	NA	0.54
Intercept	Any family psychiatric history			0.11	0	NA	NA	0.35
Intercept	Urban/rural index			5.47	0	NA	NA	7.31
Intercept	Mother's educational qualifications			1.73	0	NA	NA	1.56
Intercept	ASO (BL)			0	0	NA	NA	0
Intercept	ASO (FU)			0	0	NA	NA	0
Intercept	AEB (BL)			0	0	NA	NA	0
Intercept	AEB (FU)			0	0	NA	NA	0
Covariate regression	ASO (BL)	Male		0.09	0.03	3.11	0.002	0.07
Covariate regression	ASO (BL)	Socioeconomic deprivation (IMD)		-0.04	0.02	-2.45	0.014	-0.06
Covariate regression	ASO (BL)	Cannabis Use at baseline		0.05	0.05	0.97	0.333	0.02
Covariate regression	ASO (BL)	Age (years)		0	0	0.09	0.926	0
Covariate regression	ASO (BL)	Non-white ethnicity		0.11	0.04	2.75	0.006	0.07

Table B.9 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	ASO (BL)	Any family psychiatric history		0.16	0.05	2.87	0.004	0.07
Covariate regression	ASO (BL)	Urban/rural index		-0.01	0.02	-0.43	0.67	-0.01
Covariate regression	ASO (BL)	Mother's educational qualifications		-0.06	0.01	-4.33	< 0.001	-0.09
Covariate regression	AEB (BL)	Male		-0.03	0.03	-1.11	0.267	-0.02
Covariate regression	AEB (BL)	Socioeconomic deprivation (IMD)		-0.05	0.02	-3.12	0.002	-0.08
Covariate regression	AEB (BL)	Cannabis Use at baseline		0.12	0.04	3.02	0.003	0.07
Covariate regression	AEB (BL)	Age (years)		-0.01	0	-3.3	0.001	-0.07
Covariate regression	AEB (BL)	Non-white ethnicity		0.12	0.04	3.25	0.001	0.09
Covariate regression	AEB (BL)	Any family psychiatric history		0.13	0.04	2.84	0.004	0.07
Covariate regression	AEB (BL)	Urban/rural index		0.04	0.02	2.03	0.042	0.05
Covariate regression	AEB (BL)	Mother's educational qualifications		-0.06	0.01	-5.25	< 0.001	-0.12
Covariate regression	ASO (FU)	Male		0.02	0.02	0.9	0.371	0.01
Covariate regression	ASO (FU)	Socioeconomic deprivation (IMD)		0	0.01	0.34	0.735	0.01
Covariate regression	ASO (FU)	Cannabis Use at baseline		0.09	0.04	2.3	0.022	0.04
Covariate regression	ASO (FU)	Age (years)		0	0	-1.19	0.233	-0.01
Covariate regression	ASO (FU)	Non-white ethnicity		-0.02	0.03	-0.69	0.491	-0.01
Covariate regression	ASO (FU)	Any family psychiatric history		-0.03	0.04	-0.68	0.494	-0.01
Covariate regression	ASO (FU)	Urban/rural index		0	0.01	-0.04	0.971	0

Table B.9 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	ASO (FU)	Mother's educational qualifications		-0.02	0.01	-1.64	0.102	-0.03
Covariate regression	AEB (FU)	Male		-0.03	0.02	-1.61	0.107	-0.03
Covariate regression	AEB (FU)	Socioeconomic deprivation (IMD)		0.01	0.01	0.72	0.469	0.02
Covariate regression	AEB (FU)	Cannabis Use at baseline		0.14	0.04	3.62	< 0.001	0.09
Covariate regression	AEB (FU)	Age (years)		0	0	-1.4	0.161	-0.02
Covariate regression	AEB (FU)	Non-white ethnicity		-0.06	0.03	-2.08	0.038	-0.05
Covariate regression	AEB (FU)	Any family psychiatric history		0.04	0.04	0.9	0.37	0.02
Covariate regression	AEB (FU)	Urban/rural index		-0.01	0.01	-1.19	0.233	-0.02
Covariate regression	AEB (FU)	Mother's educational qualifications		-0.02	0.01	-2.64	0.008	-0.05
Covariate regression	Family Relationship Quality	Male		0.03	0.05	0.61	0.541	0.01
Covariate regression	Family Relationship Quality	Socioeconomic deprivation (IMD)		-0.04	0.03	-1.39	0.166	-0.04
Covariate regression	Family Relationship Quality	Cannabis Use at baseline		-0.21	0.07	-2.88	0.004	-0.07
Covariate regression	Family Relationship Quality	Age (years)		0	0.01	0.61	0.544	0.01
Covariate regression	Family Relationship Quality	Non-white ethnicity		-0.12	0.06	-1.86	0.062	-0.05
Covariate regression	Family Relationship Quality	Any family psychiatric history		-0.13	0.08	-1.6	0.11	-0.04
Covariate regression	Family Relationship Quality	Urban/rural index		0.02	0.03	0.45	0.651	0.01

Table B.9 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	Family Relationship Quality	Mother's educational qualifications		0.06	0.02	2.72	0.006	0.06
Covariate regression	Friendship Quality	Male		0.15	0.04	3.37	0.001	0.07
Covariate regression	Friendship Quality	Socioeconomic deprivation (IMD)		-0.01	0.03	-0.27	0.79	-0.01
Covariate regression	Friendship Quality	Cannabis Use at baseline		0.27	0.07	3.89	< 0.001	0.09
Covariate regression	Friendship Quality	Age (years)		-0.02	0.01	-3.4	0.001	-0.07
Covariate regression	Friendship Quality	Non-white ethnicity		-0.14	0.06	-2.45	0.014	-0.06
Covariate regression	Friendship Quality	Any family psychiatric history		-0.14	0.08	-1.8	0.073	-0.04
Covariate regression	Friendship Quality	Urban/rural index		-0.05	0.03	-1.49	0.137	-0.04
Covariate regression	Friendship Quality	Mother's educational qualifications		0.01	0.02	0.58	0.563	0.01
Covariance	ASO (BL)	AEB (BL)		0.14	0.01	13.23	< 0.001	0.37
Covariance	ASO (FU)	AEB (FU)		0.05	0.01	8.61	< 0.001	0.41
Covariance	Family Relationship Quality	Friendship Quality		0.14	0.02	6.28	< 0.001	0.17
Covariance	AEB: Parcel 1 (BL)	AEB: Parcel 1 (FU)		0.11	0.02	6.86	< 0.001	0.23
Covariance	AEB: Parcel 2 (BL)	AEB: Parcel 2 (FU)		0.06	0.01	5.23	< 0.001	0.2
Covariance	AEB: Parcel 3 (BL)	AEB: Parcel 3 (FU)		0.08	0.01	8.09	< 0.001	0.34
Covariance	AEB: Parcel 4 (BL)	AEB: Parcel 4 (FU)		0.04	0.01	4.63	< 0.001	0.18
Covariance	AEB: Parcel 5 (BL)	AEB: Parcel 5 (FU)		0.06	0.01	6.64	< 0.001	0.33
Covariance	AEB: Parcel 6 (BL)	AEB: Parcel 6 (FU)		0.2	0.02	11.46	< 0.001	0.43
Covariance	ASO: Parcel 1 (BL)	ASO: Parcel 1 (FU)		0.11	0.01	8.56	< 0.001	0.28
Covariance	ASO: Parcel 2 (BL)	ASO: Parcel 2 (FU)		0.1	0.01	9.35	< 0.001	0.31

Table B.9 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariance	ASO: Parcel 3 (BL)	ASO: Parcel 3 (FU)		0.11	0.01	9.26	< 0.001	0.31
Covariance	ASO: Parcel 4 (BL)	ASO: Parcel 4 (FU)		0.13	0.01	10.41	< 0.001	0.36
Covariance	ASO: Parcel 5 (BL)	ASO: Parcel 5 (FU)		0.1	0.01	8.75	< 0.001	0.28
Covariance	ASO: Parcel 6 (BL)	ASO: Parcel 6 (FU)		0.07	0.02	4.18	< 0.001	0.16

Table B.9: Parameter estimates of the cross-lagged mediation model of AEB, ASO and social support fit to NSPN data with a robust maximum-likelihood estimator, with missing data estimated using full-information maximum likelihood. Parameters with the same Equality constraint label were fixed to be equal. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate.

Table B.10: Parameter estimates from cross-lagged mediation models of Asociality, Paranoid Ideation and social support

Parameter type	Factor or threshold	Item or factor	Equality constraint	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	ASO (BL)	ASO: Parcel 1 (BL)	l7	1	0	NA	NA	0.73
Loading	ASO (BL)	ASO: Parcel 2 (BL)	l8	0.91	0.03	33.9	< 0.001	0.73
Loading	ASO (BL)	ASO: Parcel 3 (BL)	l9	0.96	0.03	30.42	< 0.001	0.75
Loading	ASO (BL)	ASO: Parcel 4 (BL)	l10	0.85	0.03	27.42	< 0.001	0.69
Loading	ASO (BL)	ASO: Parcel 5 (BL)	l11	1.01	0.03	36.03	< 0.001	0.78
Loading	ASO (BL)	ASO: Parcel 6 (BL)	l12	1.43	0.04	36.23	< 0.001	0.82
Loading	ASO (FU)	ASO: Parcel 1 (FU)	l7	1	0	NA	NA	0.74
Loading	ASO (FU)	ASO: Parcel 2 (FU)	l8	0.91	0.03	33.9	< 0.001	0.74
Loading	ASO (FU)	ASO: Parcel 3 (FU)	l9	0.96	0.03	30.42	< 0.001	0.76
Loading	ASO (FU)	ASO: Parcel 4 (FU)	l10	0.85	0.03	27.42	< 0.001	0.7
Loading	ASO (FU)	ASO: Parcel 5 (FU)	l11	1.01	0.03	36.03	< 0.001	0.79
Loading	ASO (FU)	ASO: Parcel 6 (FU)	l12	1.43	0.04	36.23	< 0.001	0.83

Table B.10 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	PI (BL)	PI: Parcel 1 (BL)	l13	1	0	NA	NA	0.76
Loading	PI (BL)	PI: Parcel 2 (BL)	l14	1.06	0.03	31.99	< 0.001	0.81
Loading	PI (BL)	PI: Parcel 3 (BL)	l15	0.82	0.03	31.39	< 0.001	0.74
Loading	PI (BL)	PI: Parcel 4 (BL)	l16	1.36	0.04	34.11	< 0.001	0.84
Loading	PI (FU)	PI: Parcel 1 (FU)	l13	1	0	NA	NA	0.75
Loading	PI (FU)	PI: Parcel 2 (FU)	l14	1.06	0.03	31.99	< 0.001	0.81
Loading	PI (FU)	PI: Parcel 3 (FU)	l15	0.82	0.03	31.39	< 0.001	0.73
Loading	PI (FU)	PI: Parcel 4 (FU)	l16	1.36	0.04	34.11	< 0.001	0.83
Regression	ASO (FU)	ASO (BL)		0.7	0.03	23.79	< 0.001	0.68
Regression	ASO (FU)	PI (BL)		-0.05	0.02	-2.1	0.036	-0.06
Regression	PI (FU)	PI (BL)		0.61	0.03	18.41	< 0.001	0.62
Regression	PI (FU)	ASO (BL)		-0.03	0.04	-0.92	0.359	-0.03
Regression	ASO (FU)	Family Relationship Quality		-0.08	0.01	-5.97	< 0.001	-0.12
Regression	ASO (FU)	Friendship Quality		-0.18	0.02	-11.64	< 0.001	-0.26
Regression	PI (FU)	Family Relationship Quality		-0.1	0.02	-5.46	< 0.001	-0.13
Regression	PI (FU)	Friendship Quality		-0.15	0.02	-7.85	< 0.001	-0.2
Regression	Family Relationship Quality	ASO (BL)		-0.4	0.05	-7.72	< 0.001	-0.27
Regression	Family Relationship Quality	PI (BL)		-0.2	0.04	-4.6	< 0.001	-0.16
Regression	Friendship Quality	ASO (BL)		-0.61	0.05	-11.84	< 0.001	-0.41
Regression	Friendship Quality	PI (BL)		-0.12	0.05	-2.66	0.008	-0.09
Intercept	ASO: Parcel 1 (BL)		ia7	1.05	0.19	5.58	< 0.001	1.16
Intercept	ASO: Parcel 2 (BL)		ia8	0.96	0.17	5.57	< 0.001	1.16
Intercept	ASO: Parcel 3 (BL)		ia9	0.84	0.18	4.63	< 0.001	0.98

Table B.10 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Intercept	ASO: Parcel 4 (BL)		ia10	0.72	0.16	4.51	< 0.001	0.87
Intercept	ASO: Parcel 5 (BL)		ia11	1.15	0.19	6.03	< 0.001	1.33
Intercept	ASO: Parcel 6 (BL)		ia12	1.51	0.27	5.57	< 0.001	1.29
Intercept	PI: Parcel 1 (BL)		ia13	1.39	0.22	6.39	< 0.001	1.37
Intercept	PI: Parcel 2 (BL)		ia14	1.38	0.23	5.97	< 0.001	1.36
Intercept	PI: Parcel 3 (BL)		ia15	1.03	0.18	5.77	< 0.001	1.21
Intercept	PI: Parcel 4 (BL)		ia16	1.63	0.29	5.54	< 0.001	1.3
Intercept	ASO: Parcel 1 (FU)		ia7	1.05	0.19	5.58	< 0.001	1.14
Intercept	ASO: Parcel 2 (FU)		ia8	0.96	0.17	5.57	< 0.001	1.14
Intercept	ASO: Parcel 3 (FU)		ia9	0.84	0.18	4.63	< 0.001	0.97
Intercept	ASO: Parcel 4 (FU)		ia10	0.72	0.16	4.51	< 0.001	0.86
Intercept	ASO: Parcel 5 (FU)		ia11	1.15	0.19	6.03	< 0.001	1.3
Intercept	ASO: Parcel 6 (FU)		ia12	1.51	0.27	5.57	< 0.001	1.27
Intercept	PI: Parcel 1 (FU)		ia13	1.39	0.22	6.39	< 0.001	1.39
Intercept	PI: Parcel 2 (FU)		ia14	1.38	0.23	5.97	< 0.001	1.39
Intercept	PI: Parcel 3 (FU)		ia15	1.03	0.18	5.77	< 0.001	1.23
Intercept	PI: Parcel 4 (FU)		ia16	1.63	0.29	5.54	< 0.001	1.32
Intercept	Family Relationship Quality			-0.28	0.3	-0.95	0.342	-0.29
Intercept	Friendship Quality			0.88	0.32	2.74	0.006	0.88
Intercept	Male			0.43	0.01	33.19	< 0.001	0.87
Intercept	Socioeconomic deprivation (IMD)			0.05	0.03	1.87	0.061	0.05
Intercept	Cannabis Use at baseline			0.1	0.01	12.92	< 0.001	0.34

Table B.10 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Intercept	Age (years)			19.07	0.08	235.92	< 0.001	6.19
Intercept	Non-white ethnicity			0.21	0.01	19.92	< 0.001	0.52
Intercept	Any family psychiatric history			0.1	0.01	12.54	< 0.001	0.33
Intercept	Urban/rural index			5.49	0.02	279.51	< 0.001	7.35
Intercept	Mother's educational qualifications			1.81	0.03	63.31	< 0.001	1.66
Intercept	ASO (BL)			0	0	NA	NA	0
Intercept	ASO (FU)			0	0	NA	NA	0
Intercept	PI (BL)			0	0	NA	NA	0
Intercept	PI (FU)			0	0	NA	NA	0
Covariate regression	ASO (BL)	Male		0.07	0.04	1.85	0.064	0.05
Covariate regression	ASO (BL)	Socioeconomic deprivation (IMD)		-0.04	0.02	-1.9	0.058	-0.06
Covariate regression	ASO (BL)	Cannabis Use at baseline		-0.05	0.06	-0.79	0.431	-0.02
Covariate regression	ASO (BL)	Age (years)		0	0.01	0.11	0.913	0
Covariate regression	ASO (BL)	Non-white ethnicity		0.09	0.05	1.88	0.06	0.06
Covariate regression	ASO (BL)	Any family psychiatric history		0.13	0.07	1.94	0.053	0.06
Covariate regression	ASO (BL)	Urban/rural index		-0.04	0.03	-1.47	0.142	-0.04
Covariate regression	ASO (BL)	Mother's educational qualifications		-0.05	0.02	-2.73	0.006	-0.08
Covariate regression	PI (BL)	Male		-0.09	0.04	-2.15	0.032	-0.06
Covariate regression	PI (BL)	Socioeconomic deprivation (IMD)		-0.06	0.03	-2.49	0.013	-0.08
Covariate regression	PI (BL)	Cannabis Use at baseline		0.04	0.07	0.55	0.583	0.01

Table B.10 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	PI (BL)	Age (years)		-0.02	0.01	-3.57	< 0.001	-0.1
Covariate regression	PI (BL)	Non-white ethnicity		0.1	0.06	1.79	0.074	0.05
Covariate regression	PI (BL)	Any family psychiatric history		0.31	0.08	3.78	< 0.001	0.12
Covariate regression	PI (BL)	Urban/rural index		0.04	0.03	1.34	0.181	0.04
Covariate regression	PI (BL)	Mother's educational qualifications		-0.06	0.02	-2.8	0.005	-0.08
Covariate regression	ASO (FU)	Male		0.01	0.02	0.39	0.695	0.01
Covariate regression	ASO (FU)	Socioeconomic deprivation (IMD)		0.01	0.01	0.49	0.621	0.01
Covariate regression	ASO (FU)	Cannabis Use at baseline		0.08	0.04	1.98	0.048	0.04
Covariate regression	ASO (FU)	Age (years)		0	0	-1.51	0.131	-0.02
Covariate regression	ASO (FU)	Non-white ethnicity		0	0.03	-0.16	0.877	0
Covariate regression	ASO (FU)	Any family psychiatric history		-0.03	0.04	-0.84	0.402	-0.01
Covariate regression	ASO (FU)	Urban/rural index		0	0.01	-0.28	0.777	0
Covariate regression	ASO (FU)	Mother's educational qualifications		-0.02	0.01	-1.41	0.159	-0.02
Covariate regression	PI (FU)	Male		-0.04	0.03	-1.34	0.18	-0.03
Covariate regression	PI (FU)	Socioeconomic deprivation (IMD)		0.04	0.02	2.16	0.031	0.05
Covariate regression	PI (FU)	Cannabis Use at baseline		0.09	0.05	1.72	0.085	0.04
Covariate regression	PI (FU)	Age (years)		0	0	-0.99	0.324	-0.02
Covariate regression	PI (FU)	Non-white ethnicity		-0.03	0.04	-0.69	0.489	-0.02

Table B.10 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	PI (FU)	Any family psychiatric history		0.01	0.05	0.17	0.866	0
Covariate regression	PI (FU)	Urban/rural index		-0.03	0.02	-1.79	0.073	-0.03
Covariate regression	PI (FU)	Mother's educational qualifications		-0.03	0.01	-2.07	0.038	-0.04
Covariate regression	Family Relationship Quality	Male		0.04	0.05	0.86	0.388	0.02
Covariate regression	Family Relationship Quality	Socioeconomic deprivation (IMD)		-0.04	0.03	-1.33	0.182	-0.04
Covariate regression	Family Relationship Quality	Cannabis Use at baseline		-0.23	0.08	-2.97	0.003	-0.07
Covariate regression	Family Relationship Quality	Age (years)		0	0.01	0.11	0.913	0
Covariate regression	Family Relationship Quality	Non-white ethnicity		-0.09	0.07	-1.33	0.183	-0.04
Covariate regression	Family Relationship Quality	Any family psychiatric history		-0.1	0.09	-1.12	0.264	-0.03
Covariate regression	Family Relationship Quality	Urban/rural index		0.01	0.04	0.33	0.743	0.01
Covariate regression	Family Relationship Quality	Mother's educational qualifications		0.05	0.02	2.19	0.029	0.05
Covariate regression	Friendship Quality	Male		0.17	0.05	3.62	< 0.001	0.08
Covariate regression	Friendship Quality	Socioeconomic deprivation (IMD)		-0.01	0.03	-0.44	0.66	-0.01
Covariate regression	Friendship Quality	Cannabis Use at baseline		0.25	0.07	3.43	0.001	0.08
Covariate regression	Friendship Quality	Age (years)		-0.03	0.01	-3.84	< 0.001	-0.09
Covariate regression	Friendship Quality	Non-white ethnicity		-0.17	0.06	-2.63	0.009	-0.07

Table B.10 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Equality Constraint	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	Friendship Quality	Any family psychiatric history		-0.05	0.08	-0.58	0.561	-0.01
Covariate regression	Friendship Quality	Urban/rural index		-0.09	0.04	-2.39	0.017	-0.07
Covariate regression	Friendship Quality	Mother's educational qualifications		0	0.02	-0.07	0.944	0
Covariance	ASO (BL)	PI (BL)		0.29	0.02	15.94	< 0.001	0.59
Covariance	ASO (FU)	PI (FU)		0.1	0.01	11	< 0.001	0.56
Covariance	Family Relationship Quality	Friendship Quality		0.13	0.02	5.92	< 0.001	0.17
Covariance	ASO: Parcel 1 (BL)	ASO: Parcel 1 (FU)		0.11	0.01	7.36	< 0.001	0.28
Covariance	ASO: Parcel 2 (BL)	ASO: Parcel 2 (FU)		0.12	0.01	9.53	< 0.001	0.36
Covariance	ASO: Parcel 3 (BL)	ASO: Parcel 3 (FU)		0.09	0.01	6.84	< 0.001	0.28
Covariance	ASO: Parcel 4 (BL)	ASO: Parcel 4 (FU)		0.13	0.02	8.86	< 0.001	0.37
Covariance	ASO: Parcel 5 (BL)	ASO: Parcel 5 (FU)		0.07	0.01	5.43	< 0.001	0.23
Covariance	ASO: Parcel 6 (BL)	ASO: Parcel 6 (FU)		0.06	0.02	2.88	0.004	0.14
Covariance	PI: Parcel 1 (BL)	PI: Parcel 1 (FU)		0.14	0.02	7.7	< 0.001	0.31
Covariance	PI: Parcel 2 (BL)	PI: Parcel 2 (FU)		0.06	0.02	3.28	0.001	0.17
Covariance	PI: Parcel 3 (BL)	PI: Parcel 3 (FU)		0.09	0.01	6.32	< 0.001	0.26
Covariance	PI: Parcel 4 (BL)	PI: Parcel 4 (FU)		0.11	0.02	4.66	< 0.001	0.23

Table B.10: Parameter estimates of the cross-lagged mediation model of PI, ASO and social support fit to NSPN data with a robust maximum-likelihood estimator, with missing data estimated using full-information maximum likelihood. Parameters with the same Equality constraint label were fixed to be equal. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate.

Table B.11: Parameter estimates from structural equation model predicting future depressive symptoms

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	ASO (BL)	ASO: Parcel 1 (BL)	1	0	NA	NA	0.74
Loading	ASO (BL)	ASO: Parcel 2 (BL)	0.95	0.03	37.71	< 0.001	0.76
Loading	ASO (BL)	ASO: Parcel 3 (BL)	0.91	0.03	31.16	< 0.001	0.73
Loading	ASO (BL)	ASO: Parcel 4 (BL)	0.86	0.03	31.81	< 0.001	0.7
Loading	ASO (BL)	ASO: Parcel 5 (BL)	0.95	0.02	38.53	< 0.001	0.74
Loading	ASO (BL)	ASO: Parcel 6 (BL)	1.41	0.04	37.7	< 0.001	0.83
Loading	PI (BL)	PI: Parcel 1 (BL)	1	0	NA	NA	0.75
Loading	PI (BL)	PI: Parcel 2 (BL)	0.99	0.03	38.94	< 0.001	0.74
Loading	PI (BL)	PI: Parcel 3 (BL)	0.86	0.02	38.69	< 0.001	0.76
Loading	PI (BL)	PI: Parcel 4 (BL)	1.4	0.03	43.8	< 0.001	0.85
Loading	AEB (BL)	AEB: Parcel 1 (BL)	1	0	NA	NA	0.6
Loading	AEB (BL)	AEB: Parcel 2 (BL)	1.16	0.04	26.02	< 0.001	0.72
Loading	AEB (BL)	AEB: Parcel 3 (BL)	0.9	0.04	20.67	< 0.001	0.67
Loading	AEB (BL)	AEB: Parcel 4 (BL)	0.77	0.04	19.33	< 0.001	0.64
Loading	AEB (BL)	AEB: Parcel 5 (BL)	0.71	0.04	17.77	< 0.001	0.63
Loading	AEB (BL)	AEB: Parcel 6 (BL)	1.24	0.05	23.93	< 0.001	0.68
Regression	Depressive Symptoms (FU)	Depressive Symptoms (BL)	0.41	0.03	14	< 0.001	0.4
Regression	Depressive Symptoms (FU)	AEB (BL)	0.02	0.07	0.29	0.774	0.01
Regression	Depressive Symptoms (FU)	ASO (BL)	0.18	0.04	4.53	< 0.001	0.13
Regression	Depressive Symptoms (FU)	PI (BL)	0.21	0.05	4.22	< 0.001	0.17

Table B.11 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Intercept	ASO: Parcel 1 (BL)		0.96	0.17	5.54	< 0.001	1.02
Intercept	ASO: Parcel 2 (BL)		0.88	0.17	5.3	< 0.001	1.01
Intercept	ASO: Parcel 3 (BL)		0.72	0.16	4.55	< 0.001	0.82
Intercept	ASO: Parcel 4 (BL)		0.65	0.15	4.31	< 0.001	0.75
Intercept	ASO: Parcel 5 (BL)		1.04	0.16	6.32	< 0.001	1.17
Intercept	ASO: Parcel 6 (BL)		1.36	0.24	5.58	< 0.001	1.15
Intercept	PI: Parcel 1 (BL)		1.88	0.19	9.73	< 0.001	1.82
Intercept	PI: Parcel 2 (BL)		1.85	0.19	9.74	< 0.001	1.78
Intercept	PI: Parcel 3 (BL)		1.46	0.17	8.76	< 0.001	1.67
Intercept	PI: Parcel 4 (BL)		2.31	0.27	8.6	< 0.001	1.81
Intercept	AEB: Parcel 1 (BL)		1.28	0.14	9.19	< 0.001	1.45
Intercept	AEB: Parcel 2 (BL)		1.01	0.16	6.25	< 0.001	1.18
Intercept	AEB: Parcel 3 (BL)		0.7	0.13	5.57	< 0.001	0.99
Intercept	AEB: Parcel 4 (BL)		0.58	0.11	5.35	< 0.001	0.91
Intercept	AEB: Parcel 5 (BL)		0.46	0.1	4.64	< 0.001	0.77
Intercept	AEB: Parcel 6 (BL)		1.15	0.17	6.65	< 0.001	1.19
Intercept	Depressive Symptoms (FU)		1.75	0.22	7.85	< 0.001	1.81
Intercept	Depressive Symptoms (BL)		2.62	0.22	11.66	< 0.001	2.8
Intercept	Male		0.47	0	NA	NA	0.93
Intercept	Socioeconomic deprivation (IMD)		-0.01	0	NA	NA	-0.01
Intercept	Cannabis Use at baseline		0.12	0	NA	NA	0.38
Intercept	Age (years)		19.08	0	NA	NA	6.35

Table B.11 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Intercept	Non-white ethnicity		0.23	0	NA	NA	0.54
Intercept	Any family psychiatric history		0.11	0	NA	NA	0.35
Intercept	Urban/rural index		5.47	0	NA	NA	7.31
Intercept	Mother's educational qualifications		1.73	0	NA	NA	1.56
Intercept	ASO (BL)		0	0	NA	NA	0
Intercept	PI (BL)		0	0	NA	NA	0
Intercept	AEB (BL)		0	0	NA	NA	0
Covariate regression	ASO (BL)	Male	0.1	0.03	3.14	0.002	0.07
Covariate regression	ASO (BL)	Socioeconomic deprivation (IMD)	-0.04	0.02	-2.34	0.019	-0.06
Covariate regression	ASO (BL)	Cannabis Use at baseline	0.05	0.05	1	0.318	0.02
Covariate regression	ASO (BL)	Age (years)	0	0.01	0	0.997	0
Covariate regression	ASO (BL)	Non-white ethnicity	0.11	0.04	2.69	0.007	0.07
Covariate regression	ASO (BL)	Any family psychiatric history	0.16	0.05	2.9	0.004	0.07
Covariate regression	ASO (BL)	Urban/rural index	-0.01	0.02	-0.47	0.638	-0.01
Covariate regression	ASO (BL)	Mother's educational qualifications	-0.06	0.01	-4.39	$<$ 0.001	-0.1
Covariate regression	PI (BL)	Male	-0.09	0.03	-2.54	0.011	-0.06
Covariate regression	PI (BL)	Socioeconomic deprivation (IMD)	-0.04	0.02	-2.05	0.04	-0.05
Covariate regression	PI (BL)	Cannabis Use at baseline	0.12	0.05	2.27	0.023	0.05
Covariate regression	PI (BL)	Age (years)	-0.03	0.01	-5.93	$<$ 0.001	-0.13

Table B.11 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	PI (BL)	Non-white ethnicity	0.06	0.04	1.37	0.171	0.03
Covariate regression	PI (BL)	Any family psychiatric history	0.24	0.06	4	< 0.001	0.1
Covariate regression	PI (BL)	Urban/rural index	0	0.03	0.06	0.949	0
Covariate regression	PI (BL)	Mother's educational qualifications	-0.09	0.02	-5.94	< 0.001	-0.13
Covariate regression	AEB (BL)	Male	-0.03	0.02	-1.08	0.279	-0.02
Covariate regression	AEB (BL)	Socioeconomic deprivation (IMD)	-0.04	0.01	-2.64	0.008	-0.07
Covariate regression	AEB (BL)	Cannabis Use at baseline	0.12	0.04	3.05	0.002	0.07
Covariate regression	AEB (BL)	Age (years)	-0.02	0	-4.11	< 0.001	-0.09
Covariate regression	AEB (BL)	Non-white ethnicity	0.1	0.03	3.05	0.002	0.08
Covariate regression	AEB (BL)	Any family psychiatric history	0.12	0.04	2.86	0.004	0.07
Covariate regression	AEB (BL)	Urban/rural index	0.01	0.02	0.76	0.447	0.02
Covariate regression	AEB (BL)	Mother's educational qualifications	-0.06	0.01	-5.47	< 0.001	-0.13
Covariate regression	Depressive Symptoms (FU)	Male	-0.11	0.04	-2.96	0.003	-0.06
Covariate regression	Depressive Symptoms (FU)	Socioeconomic deprivation (IMD)	0.04	0.02	1.72	0.085	0.04
Covariate regression	Depressive Symptoms (FU)	Cannabis Use at baseline	0.16	0.06	2.72	0.007	0.05
Covariate regression	Depressive Symptoms (FU)	Age (years)	0.01	0.01	0.96	0.336	0.02
Covariate regression	Depressive Symptoms (FU)	Non-white ethnicity	0	0.05	-0.01	0.991	0

Table B.11 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	Depressive Symptoms (FU)	Any family psychiatric history	0.08	0.06	1.3	0.193	0.02
Covariate regression	Depressive Symptoms (FU)	Urban/rural index	-0.02	0.03	-0.89	0.375	-0.02
Covariate regression	Depressive Symptoms (FU)	Mother's educational qualifications	-0.01	0.02	-0.54	0.589	-0.01
Covariate regression	Depressive Symptoms (BL)	Male	-0.19	0.04	-5.15	< 0.001	-0.1
Covariate regression	Depressive Symptoms (BL)	Socioeconomic deprivation (IMD)	-0.07	0.02	-3.07	0.002	-0.07
Covariate regression	Depressive Symptoms (BL)	Cannabis Use at baseline	0.31	0.06	5.39	< 0.001	0.11
Covariate regression	Depressive Symptoms (BL)	Age (years)	0.01	0.01	0.87	0.383	0.02
Covariate regression	Depressive Symptoms (BL)	Non-white ethnicity	0.08	0.05	1.59	0.112	0.04
Covariate regression	Depressive Symptoms (BL)	Any family psychiatric history	0.44	0.07	6.57	< 0.001	0.15
Covariate regression	Depressive Symptoms (BL)	Urban/rural index	0.02	0.03	0.68	0.496	0.02
Covariate regression	Depressive Symptoms (BL)	Mother's educational qualifications	-0.06	0.02	-3.77	< 0.001	-0.08
Covariance	ASO (BL)	AEB (BL)	0.14	0.01	12.87	< 0.001	0.38
Covariance	ASO (BL)	PI (BL)	0.31	0.01	21.45	< 0.001	0.6
Covariance	PI (BL)	AEB (BL)	0.25	0.01	17.82	< 0.001	0.63
Covariance	AEB (BL)	Depressive Symptoms (BL)	0.18	0.01	13.61	< 0.001	0.38
Covariance	PI (BL)	Depressive Symptoms (BL)	0.4	0.02	22.42	< 0.001	0.58

Table B.11 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariance	ASO (BL)	Depressive Symptoms (BL)	0.35	0.02	21.9	< 0.001	0.56

Table B.11: Parameter estimates of the model of baseline depressive symptoms, ASO, PI and AEB predicting future depressive symptoms. The model was fit to NSPN data with a robust maximum-likelihood estimator, with missing data estimated using full-information maximum likelihood. Parameters with the same Equality constraint label were fixed to be equal. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate.

Table B.12: Parameter estimates from structural equation model predicting future psychiatric help-seeking

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	ASO (BL)	ASO: Parcel 1 (BL)	1	0	NA	NA	0.74
Loading	ASO (BL)	ASO: Parcel 2 (BL)	0.95	0.03	37.71	< 0.001	0.76
Loading	ASO (BL)	ASO: Parcel 3 (BL)	0.91	0.03	31.16	< 0.001	0.73
Loading	ASO (BL)	ASO: Parcel 4 (BL)	0.86	0.03	31.81	< 0.001	0.7
Loading	ASO (BL)	ASO: Parcel 5 (BL)	0.95	0.02	38.53	< 0.001	0.74
Loading	ASO (BL)	ASO: Parcel 6 (BL)	1.41	0.04	37.7	< 0.001	0.83
Loading	PI (BL)	PI: Parcel 1 (BL)	1	0	NA	NA	0.75
Loading	PI (BL)	PI: Parcel 2 (BL)	0.99	0.03	38.94	< 0.001	0.74
Loading	PI (BL)	PI: Parcel 3 (BL)	0.86	0.02	38.69	< 0.001	0.76
Loading	PI (BL)	PI: Parcel 4 (BL)	1.4	0.03	43.8	< 0.001	0.85
Loading	AEB (BL)	AEB: Parcel 1 (BL)	1	0	NA	NA	0.6
Loading	AEB (BL)	AEB: Parcel 2 (BL)	1.16	0.04	26.02	< 0.001	0.72
Loading	AEB (BL)	AEB: Parcel 3 (BL)	0.9	0.04	20.67	< 0.001	0.67
Loading	AEB (BL)	AEB: Parcel 4 (BL)	0.77	0.04	19.33	< 0.001	0.64

Table B.12 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	AEB (BL)	AEB: Parcel 5 (BL)	0.71	0.04	17.77	< 0.001	0.63
Loading	AEB (BL)	AEB: Parcel 6 (BL)	1.24	0.05	23.93	< 0.001	0.68
Regression	Depressive Symptoms (FU)	Depressive Symptoms (BL)	0.41	0.03	14	< 0.001	0.4
Regression	Depressive Symptoms (FU)	AEB (BL)	0.02	0.07	0.29	0.774	0.01
Regression	Depressive Symptoms (FU)	ASO (BL)	0.18	0.04	4.53	< 0.001	0.13
Regression	Depressive Symptoms (FU)	PI (BL)	0.21	0.05	4.22	< 0.001	0.17
Intercept	ASO: Parcel 1 (BL)		0.96	0.17	5.54	< 0.001	1.02
Intercept	ASO: Parcel 2 (BL)		0.88	0.17	5.3	< 0.001	1.01
Intercept	ASO: Parcel 3 (BL)		0.72	0.16	4.55	< 0.001	0.82
Intercept	ASO: Parcel 4 (BL)		0.65	0.15	4.31	< 0.001	0.75
Intercept	ASO: Parcel 5 (BL)		1.04	0.16	6.32	< 0.001	1.17
Intercept	ASO: Parcel 6 (BL)		1.36	0.24	5.58	< 0.001	1.15
Intercept	PI: Parcel 1 (BL)		1.88	0.19	9.73	< 0.001	1.82
Intercept	PI: Parcel 2 (BL)		1.85	0.19	9.74	< 0.001	1.78
Intercept	PI: Parcel 3 (BL)		1.46	0.17	8.76	< 0.001	1.67
Intercept	PI: Parcel 4 (BL)		2.31	0.27	8.6	< 0.001	1.81
Intercept	AEB: Parcel 1 (BL)		1.28	0.14	9.19	< 0.001	1.45
Intercept	AEB: Parcel 2 (BL)		1.01	0.16	6.25	< 0.001	1.18
Intercept	AEB: Parcel 3 (BL)		0.7	0.13	5.57	< 0.001	0.99
Intercept	AEB: Parcel 4 (BL)		0.58	0.11	5.35	< 0.001	0.91
Intercept	AEB: Parcel 5 (BL)		0.46	0.1	4.64	< 0.001	0.77

Table B.12 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Intercept	AEB: Parcel 6 (BL)		1.15	0.17	6.65	< 0.001	1.19
Intercept	Depressive Symptoms (FU)		1.75	0.22	7.85	< 0.001	1.81
Intercept	Depressive Symptoms (BL)		2.62	0.22	11.66	< 0.001	2.8
Intercept	Male		0.47	0	NA	NA	0.93
Intercept	Socioeconomic deprivation (IMD)		-0.01	0	NA	NA	-0.01
Intercept	Cannabis Use at baseline		0.12	0	NA	NA	0.38
Intercept	Age (years)		19.08	0	NA	NA	6.35
Intercept	Non-white ethnicity		0.23	0	NA	NA	0.54
Intercept	Any family psychiatric history		0.11	0	NA	NA	0.35
Intercept	Urban/rural index		5.47	0	NA	NA	7.31
Intercept	Mother's educational qualifications		1.73	0	NA	NA	1.56
Intercept	ASO (BL)		0	0	NA	NA	0
Intercept	PI (BL)		0	0	NA	NA	0
Intercept	AEB (BL)		0	0	NA	NA	0
Covariate regression	ASO (BL)	Male	0.1	0.03	3.14	0.002	0.07
Covariate regression	ASO (BL)	Socioeconomic deprivation (IMD)	-0.04	0.02	-2.34	0.019	-0.06
Covariate regression	ASO (BL)	Cannabis Use at baseline	0.05	0.05	1	0.318	0.02
Covariate regression	ASO (BL)	Age (years)	0	0.01	0	0.997	0
Covariate regression	ASO (BL)	Non-white ethnicity	0.11	0.04	2.69	0.007	0.07
Covariate regression	ASO (BL)	Any family psychiatric history	0.16	0.05	2.9	0.004	0.07

Table B.12 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	ASO (BL)	Urban/rural index	-0.01	0.02	-0.47	0.638	-0.01
Covariate regression	ASO (BL)	Mother's educational qualifications	-0.06	0.01	-4.39	< 0.001	-0.1
Covariate regression	PI (BL)	Male	-0.09	0.03	-2.54	0.011	-0.06
Covariate regression	PI (BL)	Socioeconomic deprivation (IMD)	-0.04	0.02	-2.05	0.04	-0.05
Covariate regression	PI (BL)	Cannabis Use at baseline	0.12	0.05	2.27	0.023	0.05
Covariate regression	PI (BL)	Age (years)	-0.03	0.01	-5.93	< 0.001	-0.13
Covariate regression	PI (BL)	Non-white ethnicity	0.06	0.04	1.37	0.171	0.03
Covariate regression	PI (BL)	Any family psychiatric history	0.24	0.06	4	< 0.001	0.1
Covariate regression	PI (BL)	Urban/rural index	0	0.03	0.06	0.949	0
Covariate regression	PI (BL)	Mother's educational qualifications	-0.09	0.02	-5.94	< 0.001	-0.13
Covariate regression	AEB (BL)	Male	-0.03	0.02	-1.08	0.279	-0.02
Covariate regression	AEB (BL)	Socioeconomic deprivation (IMD)	-0.04	0.01	-2.64	0.008	-0.07
Covariate regression	AEB (BL)	Cannabis Use at baseline	0.12	0.04	3.05	0.002	0.07
Covariate regression	AEB (BL)	Age (years)	-0.02	0	-4.11	< 0.001	-0.09
Covariate regression	AEB (BL)	Non-white ethnicity	0.1	0.03	3.05	0.002	0.08
Covariate regression	AEB (BL)	Any family psychiatric history	0.12	0.04	2.86	0.004	0.07
Covariate regression	AEB (BL)	Urban/rural index	0.01	0.02	0.76	0.447	0.02

Table B.12 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	AEB (BL)	Mother's educational qualifications	-0.06	0.01	-5.47	< 0.001	-0.13
Covariate regression	Depressive Symptoms (FU)	Male	-0.11	0.04	-2.96	0.003	-0.06
Covariate regression	Depressive Symptoms (FU)	Socioeconomic deprivation (IMD)	0.04	0.02	1.72	0.085	0.04
Covariate regression	Depressive Symptoms (FU)	Cannabis Use at baseline	0.16	0.06	2.72	0.007	0.05
Covariate regression	Depressive Symptoms (FU)	Age (years)	0.01	0.01	0.96	0.336	0.02
Covariate regression	Depressive Symptoms (FU)	Non-white ethnicity	0	0.05	-0.01	0.991	0
Covariate regression	Depressive Symptoms (FU)	Any family psychiatric history	0.08	0.06	1.3	0.193	0.02
Covariate regression	Depressive Symptoms (FU)	Urban/rural index	-0.02	0.03	-0.89	0.375	-0.02
Covariate regression	Depressive Symptoms (FU)	Mother's educational qualifications	-0.01	0.02	-0.54	0.589	-0.01
Covariate regression	Depressive Symptoms (BL)	Male	-0.19	0.04	-5.15	< 0.001	-0.1
Covariate regression	Depressive Symptoms (BL)	Socioeconomic deprivation (IMD)	-0.07	0.02	-3.07	0.002	-0.07
Covariate regression	Depressive Symptoms (BL)	Cannabis Use at baseline	0.31	0.06	5.39	< 0.001	0.11
Covariate regression	Depressive Symptoms (BL)	Age (years)	0.01	0.01	0.87	0.383	0.02
Covariate regression	Depressive Symptoms (BL)	Non-white ethnicity	0.08	0.05	1.59	0.112	0.04
Covariate regression	Depressive Symptoms (BL)	Any family psychiatric history	0.44	0.07	6.57	< 0.001	0.15

Table B.12 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Covariate regression	Depressive Symptoms (BL)	Urban/rural index	0.02	0.03	0.68	0.496	0.02
Covariate regression	Depressive Symptoms (BL)	Mother's educational qualifications	-0.06	0.02	-3.77	< 0.001	-0.08
Covariance	ASO (BL)	AEB (BL)	0.14	0.01	12.87	< 0.001	0.38
Covariance	ASO (BL)	PI (BL)	0.31	0.01	21.45	< 0.001	0.6
Covariance	PI (BL)	AEB (BL)	0.25	0.01	17.82	< 0.001	0.63
Covariance	AEB (BL)	Depressive Symptoms (BL)	0.18	0.01	13.61	< 0.001	0.38
Covariance	PI (BL)	Depressive Symptoms (BL)	0.4	0.02	22.42	< 0.001	0.58
Covariance	ASO (BL)	Depressive Symptoms (BL)	0.35	0.02	21.9	< 0.001	0.56

Table B.12: Parameter estimates of the model of baseline psychiatric help-seeking, ASO, PI and AEB predicting future help-seeking. The model was fit to NSPN data with a robust maximum-likelihood estimator, with missing data estimated using full-information maximum likelihood. Parameters with the same Equality constraint label were fixed to be equal. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate.

B.4 Parameter estimates from structural equation models in Chapter 9

Table B.13: Parameter estimates structural equation model of childhood adversity predicting depressive symptoms and psychotic phenomena in ROOTS.

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	SMFQ: 1	DS	1.00	0.00	NA	NA	0.61
Loading	SMFQ: 2	DS	1.00	0.05	18.71	< 0.001	0.61
Loading	SMFQ: 3	DS	0.84	0.07	11.54	< 0.001	0.42
Loading	SMFQ: 4	DS	0.77	0.07	10.37	< 0.001	0.38
Loading	SMFQ: 5	DS	1.23	0.07	17.09	< 0.001	0.75

Table B.13 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	SMFQ: 6	DS	1.00	0.07	14.02	< 0.001	0.58
Loading	SMFQ: 7	DS	1.14	0.07	16.02	< 0.001	0.59
Loading	SMFQ: 8	DS	1.08	0.07	15.25	< 0.001	0.73
Loading	SMFQ: 9	DS	0.72	0.07	9.95	< 0.001	0.58
Loading	SMFQ: 10	DS	1.33	0.07	17.97	< 0.001	0.69
Loading	SMFQ: 11	DS	0.95	0.07	13.23	< 0.001	0.66
Loading	SMFQ: 12	DS	1.16	0.08	14.37	< 0.001	0.64
Loading	SMFQ: 13	DS	1.05	0.07	14.17	< 0.001	0.69
Loading	AEB: 1	AEB	1.00	0.00	NA	NA	0.72
Loading	AEB: 2	AEB	0.80	0.07	12.27	< 0.001	0.61
Loading	AEB: 3	AEB	0.63	0.08	8.27	< 0.001	0.56
Loading	AEB: 4	AEB	0.39	0.07	5.87	< 0.001	0.36
Loading	AEB: 5	AEB	0.38	0.06	6.26	< 0.001	0.49
Loading	AEB: 6	AEB	0.44	0.06	7.71	< 0.001	0.51
Loading	AEB: 7	AEB	0.96	0.05	19.94	< 0.001	0.71
Loading	AEB: 8	AEB	0.38	0.05	7.20	< 0.001	0.53
Loading	PI: 1	PI	1.00	0.00	NA	NA	0.73
Loading	PI: 2	PI	0.98	0.05	18.21	< 0.001	0.75
Loading	PI: 3	PI	0.74	0.05	15.24	< 0.001	0.66
Loading	PI: 4	PI	1.14	0.05	24.88	< 0.001	0.86
Loading	PI: 5	PI	0.73	0.05	14.02	< 0.001	0.57
Regression	DS	CA	0.06	0.01	4.33	< 0.001	0.17
Regression	AEB	CA	0.06	0.02	2.53	0.011	0.11
Regression	PI	CA	0.06	0.02	2.77	0.006	0.11
Covariate Regression	CA	Male	0.02	0.06	0.42	0.678	0.01
Covariate Regression	CA	Low socioeconomic status	0.46	0.11	4.19	< 0.001	0.16
Covariate Regression	CA	Non-white ethnicity	0.08	0.13	0.58	0.565	0.02
Covariate Regression	CA	Cannabis use at 17	0.04	0.12	0.34	0.737	0.01
Covariate Regression	CA	Mother's years of education post-16	-0.06	0.01	-5.11	< 0.001	-0.15
Covariate Regression	CA	Family psychiatric history	0.68	0.08	8.15	< 0.001	0.27
Covariate Regression	DS	Male	-0.14	0.02	-6.03	< 0.001	-0.21
Covariate Regression	DS	Low socioeconomic status	0.02	0.04	0.49	0.622	0.02
Covariate Regression	DS	Non-white ethnicity	0.07	0.05	1.30	0.194	0.05

Table B.13 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Covariate Regression	DS	Cannabis use at 17	0.09	0.03	2.56	0.01	0.08
Covariate Regression	DS	Mother's years of education post-16	0.01	0.00	1.50	0.133	0.05
Covariate Regression	DS	Family psychiatric history	0.04	0.03	1.38	0.166	0.05
Covariate Regression	AEB	Male	-0.14	0.04	-3.19	0.001	-0.14
Covariate Regression	AEB	Low socioeconomic status	0.10	0.07	1.52	0.127	0.07
Covariate Regression	AEB	Non-white ethnicity	-0.05	0.07	-0.79	0.427	-0.03
Covariate Regression	AEB	Cannabis use at 17	0.13	0.06	2.40	0.016	0.08
Covariate Regression	AEB	Mother's years of education post-16	-0.02	0.01	-2.15	0.032	-0.08
Covariate Regression	AEB	Family psychiatric history	0.12	0.06	2.19	0.029	0.10
Covariate Regression	PI	Male	-0.15	0.04	-3.90	< 0.001	-0.13
Covariate Regression	PI	Low socioeconomic status	0.11	0.06	1.80	0.072	0.07
Covariate Regression	PI	Non-white ethnicity	-0.03	0.08	-0.42	0.674	-0.01
Covariate Regression	PI	Cannabis use at 17	0.19	0.06	3.14	0.002	0.11
Covariate Regression	PI	Mother's years of education post-16	0.00	0.01	-0.35	0.728	-0.01
Covariate Regression	PI	Family psychiatric history	0.09	0.05	1.79	0.073	0.07
Residual		SMFQ: 1	0.18	0.01	26.05	< 0.001	0.62
Residual		SMFQ: 2	0.19	0.01	19.17	< 0.001	0.62
Residual		SMFQ: 3	0.36	0.01	24.37	< 0.001	0.82
Residual		SMFQ: 4	0.38	0.02	23.38	< 0.001	0.85
Residual		SMFQ: 5	0.13	0.01	13.51	< 0.001	0.44
Residual		SMFQ: 6	0.22	0.01	16.90	< 0.001	0.66
Residual		SMFQ: 7	0.27	0.01	22.15	< 0.001	0.65
Residual		SMFQ: 8	0.11	0.01	12.02	< 0.001	0.46
Residual		SMFQ: 9	0.11	0.01	15.07	< 0.001	0.67
Residual		SMFQ: 10	0.22	0.01	15.61	< 0.001	0.53
Residual		SMFQ: 11	0.13	0.01	12.50	< 0.001	0.56
Residual		SMFQ: 12	0.21	0.01	15.94	< 0.001	0.59

Table B.13 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Residual		SMFQ: 13	0.13	0.01	14.21	< 0.001	0.52
Residual		AEB: 1	0.24	0.03	9.53	< 0.001	0.49
Residual		AEB: 2	0.27	0.02	12.92	< 0.001	0.63
Residual		AEB: 3	0.22	0.02	12.22	< 0.001	0.69
Residual		AEB: 4	0.26	0.02	11.14	< 0.001	0.87
Residual		AEB: 5	0.11	0.01	8.38	< 0.001	0.76
Residual		AEB: 6	0.13	0.01	9.04	< 0.001	0.74
Residual		AEB: 7	0.23	0.02	9.57	< 0.001	0.50
Residual		AEB: 8	0.09	0.01	8.46	< 0.001	0.72
Residual		PI: 1	0.27	0.02	14.34	< 0.001	0.47
Residual		PI: 2	0.22	0.02	13.78	< 0.001	0.43
Residual		PI: 3	0.21	0.01	15.55	< 0.001	0.56
Residual		PI: 4	0.14	0.01	9.54	< 0.001	0.26
Residual		PI: 5	0.33	0.02	16.92	< 0.001	0.67
Residual		CA	0.87	0.05	17.93	< 0.001	0.86
Residual		DS	0.10	0.01	10.23	< 0.001	0.91
Residual		AEB	0.23	0.03	9.07	< 0.001	0.93
Residual		PI	0.29	0.02	13.41	< 0.001	0.94
Covariance	DS	AEB	0.05	0.01	6.42	< 0.001	0.33
Covariance	DS	PI	0.10	0.01	10.61	< 0.001	0.56
Covariance	AEB	PI	0.12	0.01	9.27	< 0.001	0.45
Intercept		SMFQ: 1	1.82	0.02	73.41	< 0.001	3.36
Intercept		SMFQ: 2	1.41	0.03	55.62	< 0.001	2.60
Intercept		SMFQ: 3	1.85	0.03	71.65	< 0.001	2.78
Intercept		SMFQ: 4	1.65	0.03	64.86	< 0.001	2.47
Intercept		SMFQ: 5	1.32	0.03	45.94	< 0.001	2.41
Intercept		SMFQ: 6	1.35	0.03	49.23	< 0.001	2.34
Intercept		SMFQ: 7	1.77	0.03	60.88	< 0.001	2.73
Intercept		SMFQ: 8	1.23	0.03	47.40	< 0.001	2.49
Intercept		SMFQ: 9	1.18	0.02	62.12	< 0.001	2.86
Intercept		SMFQ: 10	1.49	0.03	46.19	< 0.001	2.31
Intercept		SMFQ: 11	1.20	0.02	49.26	< 0.001	2.51
Intercept		SMFQ: 12	1.39	0.03	50.19	< 0.001	2.31
Intercept		SMFQ: 13	1.28	0.03	51.31	< 0.001	2.54
Intercept		AEB: 1	1.46	0.04	36.62	< 0.001	2.08
Intercept		AEB: 2	1.39	0.03	41.44	< 0.001	2.12
Intercept		AEB: 3	1.27	0.03	46.03	< 0.001	2.25
Intercept		AEB: 4	1.23	0.02	56.48	< 0.001	2.25
Intercept		AEB: 5	1.13	0.02	68.01	< 0.001	2.94
Intercept		AEB: 6	1.17	0.02	61.80	< 0.001	2.73
Intercept		AEB: 7	1.43	0.04	36.01	< 0.001	2.11
Intercept		AEB: 8	1.11	0.02	62.77	< 0.001	3.11

Table B.13 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Intercept		PI: 1	1.86	0.04	47.98	< 0.001	2.46
Intercept		PI: 2	1.57	0.04	40.28	< 0.001	2.18
Intercept		PI: 3	1.34	0.03	42.71	< 0.001	2.18
Intercept		PI: 4	1.70	0.04	39.85	< 0.001	2.32
Intercept		PI: 5	1.51	0.03	46.79	< 0.001	2.15
Intercept		CA	-0.05	0.06	-0.87	0.385	-0.05
Intercept		DS	0.00	0.00	NA	NA	0.00
Intercept		AEB	0.00	0.00	NA	NA	0.00
Intercept		PI	0.00	0.00	NA	NA	0.00
Intercept		Male	0.46	0.00	NA	NA	0.91
Intercept		Low socioeconomic status	0.14	0.00	NA	NA	0.41
Intercept		Non-white ethnicity	0.06	0.00	NA	NA	0.25
Intercept		Cannabis use at 17	0.11	0.00	NA	NA	0.36
Intercept		Mother's years of education post-16	2.41	0.00	NA	NA	1.00
Intercept		Family psychiatric history	0.20	0.00	NA	NA	0.49

Table B.13: Parameter estimates of structural equation model of childhood adversity predicting depressive symptoms and psychotic phenomena fit to ROOTS data with a robust maximum-likelihood estimator. Missing data were estimated using full-information maximum likelihood. Parameters with the same Equality constraint label were fixed to be equal. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate.

Table B.14: Parameter estimates structural equation model of childhood adversity predicting depressive symptoms and psychotic phenomena in NSPN.

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	SMFQ: 1	DS	1.00	0.00	NA	NA	0.59
Loading	SMFQ: 2	SMFQ	1.17	0.05	22.22	< 0.001	0.66
Loading	SMFQ: 3	SMFQ	0.97	0.06	15.24	< 0.001	0.47
Loading	SMFQ: 4	SMFQ	0.95	0.07	14.43	< 0.001	0.45
Loading	SMFQ: 5	SMFQ	1.58	0.07	22.20	< 0.001	0.80
Loading	SMFQ: 6	SMFQ	0.88	0.06	13.57	< 0.001	0.49
Loading	SMFQ: 7	SMFQ	1.43	0.07	21.37	< 0.001	0.66
Loading	SMFQ: 8	SMFQ	1.44	0.07	20.10	< 0.001	0.76
Loading	SMFQ: 9	SMFQ	1.10	0.07	16.56	< 0.001	0.65

Table B.14 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	SMFQ: 10	SMFQ	1.59	0.07	22.08	< 0.001	0.70
Loading	SMFQ: 11	SMFQ	1.31	0.08	16.88	< 0.001	0.70
Loading	SMFQ: 12	SMFQ	1.58	0.08	19.86	< 0.001	0.71
Loading	SMFQ: 13	SMFQ	1.35	0.07	19.03	< 0.001	0.74
Loading	AEB: 1	AEB	1.00	0.00	NA	NA	0.41
Loading	AEB: 2	AEB	0.85	0.11	7.40	< 0.001	0.46
Loading	AEB: 3	AEB	1.21	0.12	10.18	< 0.001	0.46
Loading	AEB: 4	AEB	0.83	0.11	7.91	< 0.001	0.51
Loading	AEB: 5	AEB	1.37	0.13	10.53	< 0.001	0.60
Loading	AEB: 6	AEB	0.95	0.10	9.45	< 0.001	0.47
Loading	AEB: 7	AEB	0.45	0.07	6.17	< 0.001	0.36
Loading	AEB: 8	AEB	1.03	0.08	12.25	< 0.001	0.52
Loading	AEB: 9	AEB	0.97	0.12	8.30	< 0.001	0.51
Loading	AEB: 10	AEB	0.65	0.09	7.42	< 0.001	0.36
Loading	AEB: 11	AEB	0.70	0.06	10.85	< 0.001	0.49
Loading	AEB: 12	AEB	0.34	0.06	5.55	< 0.001	0.31
Loading	AEB: 13	AEB	0.66	0.09	7.73	< 0.001	0.52
Loading	AEB: 14	AEB	0.68	0.09	7.37	< 0.001	0.49
Loading	AEB: 15	AEB	0.55	0.08	7.37	< 0.001	0.47
Loading	AEB: 16	AEB	0.88	0.10	8.96	< 0.001	0.42
Loading	AEB: 17	AEB	1.17	0.12	9.52	< 0.001	0.52
Loading	AEB: 18	AEB	1.18	0.12	10.20	< 0.001	0.54
Loading	PI: 1	PI	1.00	0.00	NA	NA	0.68
Loading	PI: 2	PI	0.77	0.04	17.54	< 0.001	0.52
Loading	PI: 3	PI	0.65	0.04	15.62	< 0.001	0.52
Loading	PI: 4	PI	0.79	0.04	20.61	< 0.001	0.50
Loading	PI: 5	PI	0.78	0.04	19.84	< 0.001	0.59
Loading	PI: 6	PI	0.74	0.04	18.29	< 0.001	0.59
Loading	PI: 7	PI	0.79	0.04	18.24	< 0.001	0.57
Loading	PI: 8	PI	0.30	0.04	8.13	< 0.001	0.39
Loading	PI: 9	PI	0.93	0.03	27.16	< 0.001	0.67
Loading	PI: 10	PI	0.63	0.04	16.24	< 0.001	0.61
Loading	PI: 11	PI	0.98	0.04	26.01	< 0.001	0.69
Loading	PI: 12	PI	1.10	0.03	36.96	< 0.001	0.74
Loading	PI: 13	PI	0.72	0.04	17.07	< 0.001	0.54
Regression	DS	CA	0.11	0.01	10.12	< 0.001	0.34
Regression	PI	CA	0.10	0.01	10.63	< 0.001	0.32
Regression	AEB	CA	0.04	0.01	6.37	< 0.001	0.25
Covariate Regression	DS	Age (years)	-0.01	0.00	-1.77	< 0.001	-0.05
Covariate Regression	DS	Male	-0.03	0.02	-1.92	< 0.001	-0.05

Table B.14 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Covariate Regression	DS	Socioeconomic Deprivation (rank)	-0.01	0.01	-0.59	< 0.001	-0.02
Covariate Regression	DS	Non-white ethnicity	-0.03	0.02	-1.18	< 0.001	-0.03
Covariate Regression	DS	Mother's educational qualifications	-0.02	0.01	-2.26	< 0.001	-0.06
Covariate Regression	DS	Urban-rural index	0.00	0.01	-0.03	< 0.001	0.00
Covariate Regression	DS	Family psychiatric history	0.09	0.03	2.77	< 0.001	0.09
Covariate Regression	DS	Cannabis use	0.04	0.03	1.67	< 0.001	0.05
Covariate Regression	PI	Age (years)	-0.01	0.00	-1.47	< 0.001	-0.04
Covariate Regression	PI	Male	-0.03	0.02	-1.81	< 0.001	-0.05
Covariate Regression	PI	Socioeconomic Deprivation (rank)	0.01	0.01	0.73	< 0.001	0.02
Covariate Regression	PI	Non-white ethnicity	-0.02	0.02	-0.68	< 0.001	-0.02
Covariate Regression	PI	Mother's educational qualifications	-0.04	0.01	-4.57	< 0.001	-0.13
Covariate Regression	PI	Urban-rural index	0.02	0.01	1.08	< 0.001	0.03
Covariate Regression	PI	Family psychiatric history	0.04	0.03	1.17	< 0.001	0.04
Covariate Regression	PI	Cannabis use	0.00	0.02	0.15	< 0.001	0.00
Covariate Regression	AEB	Age (years)	0.00	0.00	-0.78	< 0.001	-0.02
Covariate Regression	AEB	Male	-0.01	0.01	-1.38	< 0.001	-0.04
Covariate Regression	AEB	Socioeconomic Deprivation (rank)	-0.01	0.01	-1.91	< 0.001	-0.07
Covariate Regression	AEB	Non-white ethnicity	-0.01	0.01	-0.85	< 0.001	-0.03
Covariate Regression	AEB	Mother's educational qualifications	-0.02	0.00	-3.85	< 0.001	-0.11
Covariate Regression	AEB	Urban-rural index	0.01	0.01	1.67	< 0.001	0.06

Table B.14 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Covariate Regression	AEB	Family psychiatric history	0.03	0.02	1.40	< 0.001	0.05
Covariate Regression	AEB	Cannabis use	0.05	0.02	2.64	< 0.001	0.10
Covariate Regression	CA	Age (years)	0.01	0.01	1.24	< 0.001	0.03
Covariate Regression	CA	Male	-0.04	0.05	-0.90	< 0.001	-0.02
Covariate Regression	CA	Socioeconomic Deprivation (rank)	-0.10	0.03	-3.58	< 0.001	-0.10
Covariate Regression	CA	Non-white ethnicity	0.15	0.06	2.27	< 0.001	0.06
Covariate Regression	CA	Mother's educational qualifications	-0.09	0.02	-3.98	< 0.001	-0.09
Covariate Regression	CA	Urban-rural index	0.04	0.04	1.09	< 0.001	0.03
Covariate Regression	CA	Family psychiatric history	0.49	0.08	6.03	< 0.001	0.15
Covariate Regression	CA	Cannabis use	0.15	0.07	2.28	< 0.001	0.05
Residual		SMFQ: 1	0.19	0.01	31.55	< 0.001	0.65
Residual		SMFQ: 2	0.19	0.01	22.43	< 0.001	0.57
Residual		SMFQ: 3	0.35	0.01	29.75	< 0.001	0.78
Residual		SMFQ: 4	0.38	0.01	29.09	< 0.001	0.80
Residual		SMFQ: 5	0.15	0.01	18.52	< 0.001	0.37
Residual		SMFQ: 6	0.25	0.01	19.96	< 0.001	0.76
Residual		SMFQ: 7	0.28	0.01	26.85	< 0.001	0.57
Residual		SMFQ: 8	0.15	0.01	17.89	< 0.001	0.42
Residual		SMFQ: 9	0.17	0.01	18.46	< 0.001	0.58
Residual		SMFQ: 10	0.28	0.01	23.76	< 0.001	0.51
Residual		SMFQ: 11	0.18	0.01	17.21	< 0.001	0.50
Residual		SMFQ: 12	0.26	0.01	21.15	< 0.001	0.50
Residual		SMFQ: 13	0.15	0.01	16.75	< 0.001	0.45
Residual		AEB: 1	0.16	0.01	24.74	< 0.001	0.83
Residual		AEB: 2	0.09	0.01	15.37	< 0.001	0.79
Residual		AEB: 3	0.18	0.01	28.60	< 0.001	0.79
Residual		AEB: 4	0.06	0.00	13.18	< 0.001	0.74
Residual		AEB: 5	0.11	0.01	18.07	< 0.001	0.64
Residual		AEB: 6	0.10	0.01	17.90	< 0.001	0.78
Residual		AEB: 7	0.05	0.00	9.99	< 0.001	0.87
Residual		AEB: 8	0.09	0.01	16.51	< 0.001	0.73
Residual		AEB: 9	0.09	0.01	14.52	< 0.001	0.74

Table B.14 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Residual		AEB: 10	0.09	0.01	16.17	< 0.001	0.87
Residual		AEB: 11	0.05	0.00	12.24	< 0.001	0.76
Residual		AEB: 12	0.04	0.00	8.34	< 0.001	0.90
Residual		AEB: 13	0.04	0.00	11.22	< 0.001	0.73
Residual		AEB: 14	0.05	0.00	11.67	< 0.001	0.76
Residual		AEB: 15	0.04	0.00	10.14	< 0.001	0.78
Residual		AEB: 16	0.12	0.01	19.10	< 0.001	0.83
Residual		AEB: 17	0.12	0.01	18.49	< 0.001	0.73
Residual		AEB: 18	0.11	0.01	17.77	< 0.001	0.71
Residual		PI: 1	0.12	0.01	20.03	< 0.001	0.54
Residual		PI: 2	0.17	0.01	25.94	< 0.001	0.73
Residual		PI: 3	0.11	0.01	20.25	< 0.001	0.73
Residual		PI: 4	0.18	0.01	32.44	< 0.001	0.75
Residual		PI: 5	0.12	0.01	20.10	< 0.001	0.65
Residual		PI: 6	0.11	0.01	19.77	< 0.001	0.66
Residual		PI: 7	0.14	0.01	21.78	< 0.001	0.68
Residual		PI: 8	0.05	0.00	11.26	< 0.001	0.85
Residual		PI: 9	0.11	0.01	17.74	< 0.001	0.54
Residual		PI: 10	0.07	0.00	17.15	< 0.001	0.63
Residual		PI: 11	0.10	0.01	19.13	< 0.001	0.52
Residual		PI: 12	0.10	0.01	17.50	< 0.001	0.46
Residual		PI: 13	0.13	0.01	21.73	< 0.001	0.71
Residual		CA	0.96	0.03	27.58	< 0.001	0.95
Residual		DS	0.09	0.01	11.22	< 0.001	0.85
Residual		AEB	0.03	0.00	6.43	< 0.001	0.89
Residual		PI	0.09	0.01	16.12	< 0.001	0.86
Covariance	DS	AEB	0.02	0.00	7.28	< 0.001	0.37
Covariance	DS	PI	0.05	0.00	13.17	< 0.001	0.58
Covariance	AEB	PI	0.03	0.00	9.57	< 0.001	0.57
Intercepts		SMFQ: 1	1.00	0.10	10.08	< 0.001	1.84
Intercepts		SMFQ: 2	0.60	0.12	5.19	< 0.001	1.05
Intercepts		SMFQ: 3	0.98	0.10	9.96	< 0.001	1.46
Intercepts		SMFQ: 4	0.85	0.10	8.78	< 0.001	1.23
Intercepts		SMFQ: 5	0.67	0.16	4.24	< 0.001	1.04
Intercepts		SMFQ: 6	0.45	0.09	5.11	< 0.001	0.78
Intercepts		SMFQ: 7	1.02	0.14	7.10	< 0.001	1.44
Intercepts		SMFQ: 8	0.57	0.14	3.99	< 0.001	0.93
Intercepts		SMFQ: 9	0.47	0.11	4.25	< 0.001	0.85
Intercepts		SMFQ: 10	0.96	0.16	6.07	< 0.001	1.30
Intercepts		SMFQ: 11	0.51	0.13	3.85	< 0.001	0.84
Intercepts		SMFQ: 12	0.80	0.16	5.09	< 0.001	1.11
Intercepts		SMFQ: 13	0.54	0.13	4.03	< 0.001	0.92

Table B.14 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Intercepts		AEB: 1	0.25	0.07	3.77	< 0.001	0.56
Intercepts		AEB: 2	0.12	0.06	2.10	< 0.001	0.35
Intercepts		AEB: 3	0.33	0.08	4.12	< 0.001	0.69
Intercepts		AEB: 4	0.08	0.05	1.54	< 0.001	0.29
Intercepts		AEB: 5	0.20	0.09	2.24	< 0.001	0.48
Intercepts		AEB: 6	0.14	0.06	2.33	< 0.001	0.40
Intercepts		AEB: 7	0.05	0.03	1.61	< 0.001	0.21
Intercepts		AEB: 8	0.13	0.07	1.99	< 0.001	0.37
Intercepts		AEB: 9	0.13	0.06	1.99	< 0.001	0.36
Intercepts		AEB: 10	0.11	0.04	2.61	< 0.001	0.34
Intercepts		AEB: 11	0.06	0.05	1.39	< 0.001	0.24
Intercepts		AEB: 12	0.04	0.02	1.61	< 0.001	0.18
Intercepts		AEB: 13	0.05	0.04	1.05	< 0.001	0.20
Intercepts		AEB: 14	0.06	0.04	1.28	< 0.001	0.23
Intercepts		AEB: 15	0.04	0.04	1.11	< 0.001	0.19
Intercepts		AEB: 16	0.16	0.06	2.77	< 0.001	0.42
Intercepts		AEB: 17	0.19	0.08	2.47	< 0.001	0.47
Intercepts		AEB: 18	0.17	0.08	2.28	< 0.001	0.44
Intercepts		PI: 1	0.41	0.11	3.65	< 0.001	0.88
Intercepts		PI: 2	0.42	0.09	4.78	< 0.001	0.87
Intercepts		PI: 3	0.25	0.07	3.42	< 0.001	0.64
Intercepts		PI: 4	0.52	0.09	5.80	< 0.001	1.04
Intercepts		PI: 5	0.30	0.09	3.38	< 0.001	0.71
Intercepts		PI: 6	0.27	0.08	3.18	< 0.001	0.66
Intercepts		PI: 7	0.34	0.09	3.83	< 0.001	0.77
Intercepts		PI: 8	0.09	0.03	2.65	< 0.001	0.37
Intercepts		PI: 9	0.35	0.11	3.27	< 0.001	0.78
Intercepts		PI: 10	0.18	0.07	2.57	< 0.001	0.55
Intercepts		PI: 11	0.37	0.11	3.31	< 0.001	0.81
Intercepts		PI: 12	0.44	0.12	3.54	< 0.001	0.92
Intercepts		PI: 13	0.30	0.08	3.67	< 0.001	0.70
Intercepts		Age (years)	20.07	0.00	NA	NA	8.05
Intercepts		Male	0.47	0.00	NA	NA	0.94
Intercepts		Socioeconomic Deprivation (rank)	-0.04	0.00	NA	NA	-0.04
Intercepts		Non-white ethnicity	0.23	0.00	NA	NA	0.55
Intercepts		Mother's educational qualifications	1.67	0.00	NA	NA	1.51
Intercepts		Urban-rural index	5.43	0.00	NA	NA	7.36

Table B.14 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Intercepts		Family psychiatric history	0.11	0.00	NA	NA	0.35
Intercepts		Cannabis use	0.15	0.00	NA	NA	0.42
Intercepts		CA	-0.33	0.29	-1.13	< 0.001	-0.33
Intercepts		DS	0.00	0.00	NA	NA	0.00
Intercepts		AEB	0.00	0.00	NA	NA	0.00
Intercepts		PI	0.00	0.00	NA	NA	0.00

Table B.14: Parameter estimates of structural equation model of childhood adversity predicting depressive symptoms and psychotic phenomena fit to NSPN data with a robust maximum-likelihood estimator. Missing data were estimated using full-information maximum likelihood. Parameters with the same Equality constraint label were fixed to be equal. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate.

Table B.15: Parameter estimates structural equation model of longitudinal relationships between childhood adversity, social support and depressive symptoms and psychotic phenomena in ROOTS.

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	SMFQ: 1	DS	1.00	0.00	NA	NA	0.61
Loading	SMFQ: 2	DS	1.00	0.05	18.75	< 0.001	0.61
Loading	SMFQ: 3	DS	0.84	0.07	11.59	< 0.001	0.42
Loading	SMFQ: 4	DS	0.77	0.07	10.37	< 0.001	0.39
Loading	SMFQ: 5	DS	1.23	0.07	17.14	< 0.001	0.75
Loading	SMFQ: 6	DS	1.00	0.07	13.99	< 0.001	0.58
Loading	SMFQ: 7	DS	1.14	0.07	16.03	< 0.001	0.59
Loading	SMFQ: 8	DS	1.08	0.07	15.26	< 0.001	0.73
Loading	SMFQ: 9	DS	0.71	0.07	9.96	< 0.001	0.58
Loading	SMFQ: 10	DS	1.33	0.07	17.97	< 0.001	0.69
Loading	SMFQ: 11	DS	0.95	0.07	13.25	< 0.001	0.66
Loading	SMFQ: 12	DS	1.16	0.08	14.38	< 0.001	0.64
Loading	SMFQ: 13	DS	1.05	0.07	14.16	< 0.001	0.69
Loading	AEB: 1	AEB	1.00	0.00	NA	NA	0.71
Loading	AEB: 2	AEB	0.80	0.07	12.29	< 0.001	0.61
Loading	AEB: 3	AEB	0.63	0.08	8.26	< 0.001	0.56
Loading	AEB: 4	AEB	0.39	0.07	5.87	< 0.001	0.36
Loading	AEB: 5	AEB	0.38	0.06	6.25	< 0.001	0.49
Loading	AEB: 6	AEB	0.44	0.06	7.70	< 0.001	0.51
Loading	AEB: 7	AEB	0.96	0.05	19.95	< 0.001	0.71
Loading	AEB: 8	AEB	0.38	0.05	7.20	< 0.001	0.53
Loading	PI: 1	PI	1.00	0.00	NA	NA	0.73

Table B.15 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	PI: 2	PI	0.99	0.05	18.19	< 0.001	0.75
Loading	PI: 3	PI	0.74	0.05	15.23	< 0.001	0.66
Loading	PI: 4	PI	1.14	0.05	24.85	< 0.001	0.86
Loading	PI: 5	PI	0.73	0.05	14.02	< 0.001	0.57
Regression	DS	CA	0.05	0.01	3.56	< 0.001	0.14
Regression	AEB	CA	0.05	0.02	2.29	0.022	0.10
Regression	PI	CA	0.05	0.02	2.07	0.039	0.08
Regression	DS	Family support	-0.06	0.01	-4.90	< 0.001	-0.19
Regression	DS	Friendship support	-0.04	0.01	-3.07	0.002	-0.12
Regression	AEB	Family support	-0.03	0.02	-1.72	0.085	-0.06
Regression	AEB	Friendship support	0.00	0.02	-0.20	0.844	-0.01
Regression	PI	Family support	-0.09	0.02	-4.21	< 0.001	-0.16
Regression	PI	Friendship support	-0.06	0.02	-3.04	0.002	-0.12
Regression	Family support	CA	-0.15	0.04	-4.32	< 0.001	-0.15
Regression	Friendship support	CA	-0.05	0.04	-1.19	0.235	-0.05
Cov. Reg.	Family support	Family psychiatric history	-0.07	0.08	-0.92	0.358	-0.03
Cov. Reg.	Family support	Male	0.02	0.06	0.39	0.695	0.01
Cov. Reg.	Family support	Low socioeconomic status	0.02	0.09	0.21	0.833	0.01
Cov. Reg.	Family support	Non-white ethnicity	0.06	0.13	0.45	0.653	0.01
Cov. Reg.	Family support	Cannabis use at 17	-0.35	0.12	-2.94	0.003	-0.11
Cov. Reg.	Family support	Mother's years of education post-16	0.01	0.01	0.44	0.661	0.01
Cov. Reg.	Friendship support	Family psychiatric history	-0.19	0.08	-2.28	0.023	-0.08
Cov. Reg.	Friendship support	Male	0.11	0.06	1.77	0.076	0.05
Cov. Reg.	Friendship support	Low socioeconomic status	0.00	0.09	-0.02	0.983	0.00
Cov. Reg.	Friendship support	Non-white ethnicity	-0.58	0.13	-4.36	< 0.001	-0.14
Cov. Reg.	Friendship support	Cannabis use at 17	0.04	0.11	0.34	0.733	0.01

Table B.15 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Cov. Reg.	Friendship support	Mother's years of education post-16	-0.02	0.01	-1.65	0.099	-0.05
Cov. Reg.	DS	Family psychiatric history	0.03	0.03	1.00	0.317	0.04
Cov. Reg.	DS	Male	-0.13	0.02	-6.00	< 0.001	-0.20
Cov. Reg.	DS	Low socioeconomic status	0.01	0.03	0.30	0.765	0.01
Cov. Reg.	DS	Non-white ethnicity	0.05	0.05	1.04	0.299	0.04
Cov. Reg.	DS	Cannabis use at 17	0.07	0.03	1.97	0.049	0.06
Cov. Reg.	DS	Mother's years of education post-16	0.01	0.00	1.45	0.148	0.05
Cov. Reg.	AEB	Family psychiatric history	0.12	0.06	2.12	0.034	0.09
Cov. Reg.	AEB	Male	-0.14	0.04	-3.16	0.002	-0.14
Cov. Reg.	AEB	Low socioeconomic status	0.10	0.06	1.47	0.142	0.07
Cov. Reg.	AEB	Non-white ethnicity	-0.05	0.07	-0.72	0.474	-0.02
Cov. Reg.	AEB	Cannabis use at 17	0.12	0.05	2.25	0.024	0.08
Cov. Reg.	AEB	Mother's years of education post-16	-0.02	0.01	-2.11	0.035	-0.08
Cov. Reg.	PI	Family psychiatric history	0.07	0.05	1.38	0.167	0.05
Cov. Reg.	PI	Male	-0.14	0.04	-3.81	< 0.001	-0.13
Cov. Reg.	PI	Low socioeconomic status	0.10	0.06	1.64	0.101	0.07
Cov. Reg.	PI	Non-white ethnicity	-0.06	0.07	-0.78	0.434	-0.03
Cov. Reg.	PI	Cannabis use at 17	0.16	0.06	2.66	0.008	0.09
Cov. Reg.	PI	Mother's years of education post-16	0.00	0.01	-0.46	0.642	-0.02
Cov. Reg.	CA	Family psychiatric history	0.67	0.08	8.09	< 0.001	0.26
Cov. Reg.	CA	Male	0.03	0.06	0.44	0.657	0.01
Cov. Reg.	CA	Low socioeconomic status	0.46	0.11	4.21	< 0.001	0.16
Cov. Reg.	CA	Non-white ethnicity	0.07	0.13	0.55	0.583	0.02

Table B.15 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Cov. Reg.	CA	Cannabis use at 17	0.03	0.12	0.26	0.797	0.01
Cov. Reg.	CA	Mother's years of education post-16	-0.06	0.01	-5.12	< 0.001	-0.15
Cov. Reg.		SMFQ: 1	0.18	0.01	26.14	< 0.001	0.62
Cov. Reg.		SMFQ: 2	0.19	0.01	19.16	< 0.001	0.62
Cov. Reg.		SMFQ: 3	0.36	0.01	24.38	< 0.001	0.82
Cov. Reg.		SMFQ: 4	0.38	0.02	23.36	< 0.001	0.85
Cov. Reg.		SMFQ: 5	0.13	0.01	13.59	< 0.001	0.44
Cov. Reg.		SMFQ: 6	0.22	0.01	16.93	< 0.001	0.67
Cov. Reg.		SMFQ: 7	0.27	0.01	22.16	< 0.001	0.65
Cov. Reg.		SMFQ: 8	0.11	0.01	11.99	< 0.001	0.47
Cov. Reg.		SMFQ: 9	0.11	0.01	15.07	< 0.001	0.67
Cov. Reg.		SMFQ: 10	0.22	0.01	15.62	< 0.001	0.52
Cov. Reg.		SMFQ: 11	0.13	0.01	12.54	< 0.001	0.56
Cov. Reg.		SMFQ: 12	0.21	0.01	15.97	< 0.001	0.59
Cov. Reg.		SMFQ: 13	0.13	0.01	14.26	< 0.001	0.52
Cov. Reg.		AEB: 1	0.24	0.03	9.52	< 0.001	0.49
Cov. Reg.		AEB: 2	0.27	0.02	12.91	< 0.001	0.63
Cov. Reg.		AEB: 3	0.22	0.02	12.19	< 0.001	0.69
Cov. Reg.		AEB: 4	0.26	0.02	11.14	< 0.001	0.87
Cov. Reg.		AEB: 5	0.11	0.01	8.38	< 0.001	0.76
Cov. Reg.		AEB: 6	0.13	0.01	9.04	< 0.001	0.74
Cov. Reg.		AEB: 7	0.23	0.02	9.57	< 0.001	0.50
Cov. Reg.		AEB: 8	0.09	0.01	8.46	< 0.001	0.72
Cov. Reg.		PI: 1	0.27	0.02	14.32	< 0.001	0.47
Cov. Reg.		PI: 2	0.22	0.02	13.75	< 0.001	0.43
Cov. Reg.		PI: 3	0.21	0.01	15.58	< 0.001	0.56
Cov. Reg.		PI: 4	0.14	0.01	9.54	< 0.001	0.26
Cov. Reg.		PI: 5	0.33	0.02	16.91	< 0.001	0.67
Cov. Reg.		Family support	0.96	0.05	20.80	< 0.001	0.96
Cov. Reg.		Friendship support	0.96	0.05	18.12	< 0.001	0.97
Cov. Reg.		CA	0.87	0.05	17.92	< 0.001	0.86
Cov. Reg.		DS	0.10	0.01	10.27	< 0.001	0.86
Cov. Reg.		AEB	0.23	0.03	9.07	< 0.001	0.93
Cov. Reg.		PI	0.27	0.02	13.17	< 0.001	0.90
Covariance	DS	AEB	0.05	0.01	6.32	< 0.001	0.33
Covariance	DS	PI	0.09	0.01	10.24	< 0.001	0.54
Covariance	AEB	PI	0.11	0.01	9.25	< 0.001	0.45
Covariance	Family support	Friendship support	0.20	0.03	5.67	< 0.001	0.20

Table B.15 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Intercept		SMFQ: 1	1.83	0.02	74.59	< 0.001	3.36
Intercept		SMFQ: 2	1.42	0.03	56.59	< 0.001	2.61
Intercept		SMFQ: 3	1.85	0.03	72.65	< 0.001	2.79
Intercept		SMFQ: 4	1.65	0.02	66.22	< 0.001	2.48
Intercept		SMFQ: 5	1.33	0.03	46.86	< 0.001	2.42
Intercept		SMFQ: 6	1.36	0.03	49.75	< 0.001	2.35
Intercept		SMFQ: 7	1.77	0.03	62.15	< 0.001	2.74
Intercept		SMFQ: 8	1.24	0.03	47.90	< 0.001	2.51
Intercept		SMFQ: 9	1.19	0.02	62.54	< 0.001	2.87
Intercept		SMFQ: 10	1.50	0.03	47.11	< 0.001	2.33
Intercept		SMFQ: 11	1.21	0.02	49.99	< 0.001	2.52
Intercept		SMFQ: 12	1.40	0.03	50.92	< 0.001	2.32
Intercept		SMFQ: 13	1.29	0.02	52.08	< 0.001	2.55
Intercept		AEB: 1	1.46	0.04	36.42	< 0.001	2.08
Intercept		AEB: 2	1.39	0.03	41.21	< 0.001	2.12
Intercept		AEB: 3	1.27	0.03	45.77	< 0.001	2.25
Intercept		AEB: 4	1.23	0.02	56.21	< 0.001	2.25
Intercept		AEB: 5	1.13	0.02	67.33	< 0.001	2.94
Intercept		AEB: 6	1.17	0.02	61.33	< 0.001	2.74
Intercept		AEB: 7	1.43	0.04	35.74	< 0.001	2.11
Intercept		AEB: 8	1.11	0.02	62.41	< 0.001	3.11
Intercept		PI: 1	1.87	0.04	48.66	< 0.001	2.48
Intercept		PI: 2	1.58	0.04	40.75	< 0.001	2.19
Intercept		PI: 3	1.35	0.03	43.05	< 0.001	2.19
Intercept		PI: 4	1.71	0.04	40.54	< 0.001	2.34
Intercept		PI: 5	1.51	0.03	47.07	< 0.001	2.16
Intercept		Family support	0.02	0.06	0.27	0.785	0.02
Intercept		Friendship support	0.08	0.06	1.24	0.215	0.08
Intercept		CA	-0.04	0.06	-0.80	0.425	-0.04
Intercept		Family psychiatric history	0.20	0.00	NA	NA	0.49
Intercept		Male	0.46	0.00	NA	NA	0.91
Intercept		Low socioeconomic status	0.14	0.00	NA	NA	0.41
Intercept		Non-white ethnicity	0.06	0.00	NA	NA	0.25
Intercept		Cannabis use at 17	0.11	0.00	NA	NA	0.36
Intercept		Mother's years of education post-16	2.41	0.00	NA	NA	1.00
Intercept		DS	0.00	0.00	NA	NA	0.00

Table B.15 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Intercept		AEB	0.00	0.00	NA	NA	0.00
Intercept		PI	0.00	0.00	NA	NA	0.00

Table B.15: Parameter estimates of structural equation model of relationships between childhood adversity, social support and later depressive symptoms and psychotic phenomena fit to ROOTS data with a robust maximum-likelihood estimator. Missing data were estimated using full-information maximum likelihood. Parameters with the same Equality constraint label were fixed to be equal. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate.

Table B.16: Parameter estimates structural equation model of longitudinal relationships between childhood adversity, social support and depressive symptoms and psychotic phenomena in ROOTS.

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	SMFQ: 1	DS	1.00	0.00	NA	NA	0.59
Loading	SMFQ: 2	DS	1.17	0.05	22.24	< 0.001	0.66
Loading	SMFQ: 3	DS	0.97	0.06	15.26	< 0.001	0.47
Loading	SMFQ: 4	DS	0.95	0.07	14.44	< 0.001	0.45
Loading	SMFQ: 5	DS	1.57	0.07	22.21	< 0.001	0.79
Loading	SMFQ: 6	DS	0.88	0.06	13.57	< 0.001	0.49
Loading	SMFQ: 7	DS	1.43	0.07	21.39	< 0.001	0.66
Loading	SMFQ: 8	DS	1.44	0.07	20.12	< 0.001	0.76
Loading	SMFQ: 9	DS	1.10	0.07	16.55	< 0.001	0.65
Loading	SMFQ: 10	DS	1.59	0.07	22.10	< 0.001	0.70
Loading	SMFQ: 11	DS	1.31	0.08	16.89	< 0.001	0.70
Loading	SMFQ: 12	DS	1.58	0.08	19.95	< 0.001	0.71
Loading	SMFQ: 13	DS	1.34	0.07	19.06	< 0.001	0.74
Loading	AEB: 1	AEB	1.00	0.00	NA	NA	0.41
Loading	AEB: 2	AEB	0.85	0.11	7.39	< 0.001	0.46
Loading	AEB: 3	AEB	1.21	0.12	10.15	< 0.001	0.46
Loading	AEB: 4	AEB	0.83	0.11	7.90	< 0.001	0.51
Loading	AEB: 5	AEB	1.38	0.13	10.51	< 0.001	0.60
Loading	AEB: 6	AEB	0.95	0.10	9.44	< 0.001	0.47
Loading	AEB: 7	AEB	0.45	0.07	6.16	< 0.001	0.36
Loading	AEB: 8	AEB	1.03	0.08	12.24	< 0.001	0.52
Loading	AEB: 9	AEB	0.97	0.12	8.29	< 0.001	0.51
Loading	AEB: 10	AEB	0.65	0.09	7.40	< 0.001	0.36
Loading	AEB: 11	AEB	0.70	0.06	10.85	< 0.001	0.49
Loading	AEB: 12	AEB	0.34	0.06	5.54	< 0.001	0.31
Loading	AEB: 13	AEB	0.66	0.09	7.73	< 0.001	0.52
Loading	AEB: 14	AEB	0.68	0.09	7.37	< 0.001	0.49

Table B.16 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Loading	AEB: 15	AEB	0.56	0.08	7.38	< 0.001	0.47
Loading	AEB: 16	AEB	0.88	0.10	8.96	< 0.001	0.42
Loading	AEB: 17	AEB	1.17	0.12	9.50	< 0.001	0.52
Loading	AEB: 18	AEB	1.18	0.12	10.19	< 0.001	0.54
Loading	PI: 1	PI	1.00	0.00	NA	NA	0.68
Loading	PI: 2	PI	0.77	0.04	17.52	< 0.001	0.52
Loading	PI: 3	PI	0.64	0.04	15.61	< 0.001	0.52
Loading	PI: 4	PI	0.79	0.04	20.67	< 0.001	0.50
Loading	PI: 5	PI	0.78	0.04	20.01	< 0.001	0.59
Loading	PI: 6	PI	0.74	0.04	18.30	< 0.001	0.59
Loading	PI: 7	PI	0.79	0.04	18.26	< 0.001	0.57
Loading	PI: 8	PI	0.30	0.04	8.14	< 0.001	0.39
Loading	PI: 9	PI	0.93	0.03	27.16	< 0.001	0.67
Loading	PI: 10	PI	0.63	0.04	16.31	< 0.001	0.61
Loading	PI: 11	PI	0.98	0.04	26.00	< 0.001	0.69
Loading	PI: 12	PI	1.10	0.03	36.97	< 0.001	0.74
Loading	PI: 13	PI	0.72	0.04	17.10	< 0.001	0.54
Regression	DS	CA	0.06	0.01	5.15	< 0.001	0.19
Regression	DS	Friendship support	-0.06	0.01	-5.60	< 0.001	-0.18
Regression	DS	Family support	-0.06	0.01	-6.07	< 0.001	-0.19
Regression	AEB	CA	0.04	0.01	4.72	< 0.001	0.21
Regression	AEB	Friendship support	-0.02	0.01	-3.80	< 0.001	-0.13
Regression	AEB	Family support	0.00	0.01	-0.06	0.952	0.00
Regression	PI	CA	0.06	0.01	5.93	< 0.001	0.20
Regression	PI	Friendship support	-0.07	0.01	-7.47	< 0.001	-0.23
Regression	PI	Family support	-0.03	0.01	-2.85	0.004	-0.10
Regression	Friendship support	CA	-0.29	0.02	-12.13	< 0.001	-0.29
Regression	Family support	CA	-0.51	0.02	-25.27	< 0.001	-0.51
Cov. Reg.	DS	Age (years)	0.00	0.00	-0.73	0.466	-0.02
Cov. Reg.	DS	Male	-0.03	0.02	-1.85	0.064	-0.05
Cov. Reg.	DS	Socioeconomic Deprivation (rank)	0.00	0.01	-0.41	0.679	-0.01
Cov. Reg.	DS	Non-white ethnicity	-0.02	0.02	-1.04	0.298	-0.03
Cov. Reg.	DS	Mother's educational qualifications	-0.01	0.01	-1.85	0.064	-0.05

Table B.16 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Cov. Reg.	DS	Urban-rural index	0.00	0.01	-0.06	0.948	0.00
Cov. Reg.	DS	Family psychiatric history	0.09	0.03	2.70	0.007	0.09
Cov. Reg.	DS	Cannabis use	0.05	0.02	2.30	0.021	0.06
Cov. Reg.	PI	Age (years)	0.00	0.00	-0.82	0.414	-0.02
Cov. Reg.	PI	Male	-0.03	0.02	-1.68	0.093	-0.04
Cov. Reg.	PI	Socioeconomic Deprivation (rank)	0.01	0.01	0.99	0.322	0.03
Cov. Reg.	PI	Non-white ethnicity	-0.01	0.02	-0.54	0.586	-0.02
Cov. Reg.	PI	Mother's educational qualifications	-0.03	0.01	-4.32	< 0.001	-0.12
Cov. Reg.	PI	Urban-rural index	0.01	0.01	1.06	0.288	0.03
Cov. Reg.	PI	Family psychiatric history	0.03	0.03	1.05	0.292	0.03
Cov. Reg.	PI	Cannabis use	0.02	0.02	0.96	0.335	0.03
Cov. Reg.	AEB	Age (years)	0.00	0.00	-0.63	0.529	-0.02
Cov. Reg.	AEB	Male	-0.01	0.01	-1.30	0.195	-0.04
Cov. Reg.	AEB	Socioeconomic Deprivation (rank)	-0.01	0.01	-1.79	0.073	-0.07
Cov. Reg.	AEB	Non-white ethnicity	-0.01	0.01	-0.80	0.424	-0.03
Cov. Reg.	AEB	Mother's educational qualifications	-0.02	0.00	-3.78	< 0.001	-0.11
Cov. Reg.	AEB	Urban-rural index	0.01	0.01	1.65	0.099	0.05
Cov. Reg.	AEB	Family psychiatric history	0.03	0.02	1.35	0.177	0.05
Cov. Reg.	AEB	Cannabis use	0.06	0.02	3.02	0.003	0.11
Cov. Reg.	CA	Age (years)	0.01	0.01	1.22	0.224	0.03
Cov. Reg.	CA	Male	-0.03	0.05	-0.72	0.471	-0.02
Cov. Reg.	CA	Socioeconomic Deprivation (rank)	-0.11	0.03	-3.71	< 0.001	-0.10
Cov. Reg.	CA	Non-white ethnicity	0.14	0.06	2.13	0.033	0.06
Cov. Reg.	CA	Mother's educational qualifications	-0.09	0.02	-4.02	< 0.001	-0.09

Table B.16 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Cov. Reg.	CA	Urban-rural index	0.04	0.04	1.00	0.315	0.03
Cov. Reg.	CA	Family psychiatric history	0.48	0.08	6.04	< 0.001	0.15
Cov. Reg.	CA	Cannabis use	0.16	0.06	2.45	0.014	0.06
Cov. Reg.	Friendship support	Age (years)	0.01	0.01	0.65	0.516	0.01
Cov. Reg.	Friendship support	Male	-0.05	0.05	-1.01	0.31	-0.02
Cov. Reg.	Friendship support	Socioeconomic Deprivation (rank)	0.03	0.03	0.99	0.321	0.03
Cov. Reg.	Friendship support	Non-white ethnicity	0.03	0.06	0.47	0.636	0.01
Cov. Reg.	Friendship support	Mother's educational qualifications	0.04	0.02	1.84	0.066	0.04
Cov. Reg.	Friendship support	Urban-rural index	-0.02	0.03	-0.52	0.603	-0.01
Cov. Reg.	Friendship support	Family psychiatric history	-0.07	0.08	-0.91	0.361	-0.02
Cov. Reg.	Friendship support	Cannabis use	0.27	0.06	4.28	< 0.001	0.09
Cov. Reg.	Family support	Age (years)	0.04	0.01	4.84	< 0.001	0.10
Cov. Reg.	Family support	Male	-0.02	0.04	-0.56	0.578	-0.01
Cov. Reg.	Family support	Socioeconomic Deprivation (rank)	-0.01	0.02	-0.44	0.662	-0.01
Cov. Reg.	Family support	Non-white ethnicity	0.01	0.05	0.13	0.894	0.00
Cov. Reg.	Family support	Mother's educational qualifications	0.05	0.02	2.85	0.004	0.06
Cov. Reg.	Family support	Urban-rural index	0.00	0.03	0.08	0.935	0.00
Cov. Reg.	Family support	Family psychiatric history	-0.08	0.06	-1.18	0.239	-0.02
Cov. Reg.	Family support	Cannabis use	-0.08	0.06	-1.37	0.17	-0.03
Residual		SMFQ: 1	0.19	0.01	31.55	< 0.001	0.65
Residual		SMFQ: 2	0.19	0.01	22.45	< 0.001	0.57
Residual		SMFQ: 3	0.35	0.01	29.73	< 0.001	0.78
Residual		SMFQ: 4	0.38	0.01	29.11	< 0.001	0.80

Table B.16 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Residual		SMFQ: 5	0.15	0.01	18.58	< 0.001	0.37
Residual		SMFQ: 6	0.25	0.01	19.98	< 0.001	0.76
Residual		SMFQ: 7	0.28	0.01	26.81	< 0.001	0.57
Residual		SMFQ: 8	0.15	0.01	17.99	< 0.001	0.42
Residual		SMFQ: 9	0.17	0.01	18.53	< 0.001	0.58
Residual		SMFQ: 10	0.27	0.01	23.71	< 0.001	0.51
Residual		SMFQ: 11	0.18	0.01	17.26	< 0.001	0.50
Residual		SMFQ: 12	0.26	0.01	21.17	< 0.001	0.50
Residual		SMFQ: 13	0.15	0.01	16.88	< 0.001	0.45
Residual		AEB: 1	0.16	0.01	24.73	< 0.001	0.83
Residual		AEB: 2	0.09	0.01	15.36	< 0.001	0.79
Residual		AEB: 3	0.18	0.01	28.55	< 0.001	0.79
Residual		AEB: 4	0.06	0.00	13.19	< 0.001	0.74
Residual		AEB: 5	0.11	0.01	18.07	< 0.001	0.64
Residual		AEB: 6	0.10	0.01	17.90	< 0.001	0.78
Residual		AEB: 7	0.05	0.00	9.98	< 0.001	0.87
Residual		AEB: 8	0.09	0.01	16.50	< 0.001	0.73
Residual		AEB: 9	0.09	0.01	14.50	< 0.001	0.74
Residual		AEB: 10	0.09	0.01	16.17	< 0.001	0.87
Residual		AEB: 11	0.05	0.00	12.24	< 0.001	0.76
Residual		AEB: 12	0.04	0.00	8.34	< 0.001	0.90
Residual		AEB: 13	0.04	0.00	11.22	< 0.001	0.73
Residual		AEB: 14	0.05	0.00	11.67	< 0.001	0.76
Residual		AEB: 15	0.04	0.00	10.14	< 0.001	0.78
Residual		AEB: 16	0.12	0.01	19.09	< 0.001	0.83
Residual		AEB: 17	0.12	0.01	18.48	< 0.001	0.73
Residual		AEB: 18	0.11	0.01	17.79	< 0.001	0.71
Residual		PI: 1	0.12	0.01	20.06	< 0.001	0.54
Residual		PI: 2	0.17	0.01	25.94	< 0.001	0.73
Residual		PI: 3	0.11	0.01	20.28	< 0.001	0.73
Residual		PI: 4	0.18	0.01	32.43	< 0.001	0.75
Residual		PI: 5	0.11	0.01	20.03	< 0.001	0.65
Residual		PI: 6	0.11	0.01	19.84	< 0.001	0.66
Residual		PI: 7	0.14	0.01	21.79	< 0.001	0.68
Residual		PI: 8	0.05	0.00	11.26	< 0.001	0.85
Residual		PI: 9	0.11	0.01	17.79	< 0.001	0.55
Residual		PI: 10	0.07	0.00	17.18	< 0.001	0.63
Residual		PI: 11	0.10	0.01	19.16	< 0.001	0.52
Residual		PI: 12	0.10	0.01	17.58	< 0.001	0.46
Residual		PI: 13	0.13	0.01	21.78	< 0.001	0.71
Residual		CA	0.97	0.03	27.64	< 0.001	0.95

Table B.16 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Residual		Friendship support	0.94	0.03	33.03	< 0.001	0.90
Residual		Family support	0.72	0.02	32.92	< 0.001	0.72
Residual		DS	0.08	0.01	11.21	< 0.001	0.78
Residual		AEB	0.03	0.00	6.36	< 0.001	0.88
Residual		PI	0.08	0.01	16.17	< 0.001	0.80
Covariance	Friendship support	Family support	0.21	0.02	10.52	< 0.001	0.26
Covariance	DS	AEB	0.02	0.00	7.06	< 0.001	0.35
Covariance	DS	PI	0.04	0.00	12.71	< 0.001	0.55
Covariance	AEB	PI	0.03	0.00	9.42	< 0.001	0.56
Intercept		SMFQ: 1	0.93	0.10	9.69	< 0.001	1.70
Intercept		SMFQ: 2	0.51	0.11	4.61	< 0.001	0.89
Intercept		SMFQ: 3	0.91	0.09	9.62	< 0.001	1.35
Intercept		SMFQ: 4	0.78	0.09	8.38	< 0.001	1.12
Intercept		SMFQ: 5	0.55	0.15	3.63	< 0.001	0.85
Intercept		SMFQ: 6	0.39	0.08	4.55	< 0.001	0.67
Intercept		SMFQ: 7	0.91	0.14	6.59	< 0.001	1.28
Intercept		SMFQ: 8	0.46	0.14	3.35	0.001	0.75
Intercept		SMFQ: 9	0.38	0.11	3.64	< 0.001	0.70
Intercept		SMFQ: 10	0.84	0.15	5.51	< 0.001	1.14
Intercept		SMFQ: 11	0.41	0.13	3.23	0.001	0.68
Intercept		SMFQ: 12	0.68	0.15	4.50	< 0.001	0.94
Intercept		SMFQ: 13	0.44	0.13	3.41	0.001	0.75
Intercept		AEB: 1	0.24	0.07	3.68	< 0.001	0.55
Intercept		AEB: 2	0.11	0.06	2.00	0.045	0.33
Intercept		AEB: 3	0.32	0.08	4.04	< 0.001	0.67
Intercept		AEB: 4	0.08	0.05	1.44	0.15	0.27
Intercept		AEB: 5	0.19	0.09	2.15	0.032	0.46
Intercept		AEB: 6	0.14	0.06	2.24	0.025	0.38
Intercept		AEB: 7	0.05	0.03	1.52	0.128	0.20
Intercept		AEB: 8	0.13	0.07	1.89	0.059	0.36
Intercept		AEB: 9	0.12	0.06	1.89	0.059	0.35
Intercept		AEB: 10	0.11	0.04	2.52	0.012	0.33
Intercept		AEB: 11	0.06	0.05	1.29	0.196	0.23
Intercept		AEB: 12	0.03	0.02	1.51	0.131	0.17
Intercept		AEB: 13	0.04	0.04	0.95	0.341	0.18
Intercept		AEB: 14	0.05	0.04	1.18	0.236	0.21
Intercept		AEB: 15	0.04	0.04	1.01	0.312	0.17
Intercept		AEB: 16	0.15	0.06	2.67	0.008	0.41
Intercept		AEB: 17	0.18	0.08	2.38	0.017	0.45
Intercept		AEB: 18	0.17	0.08	2.18	0.029	0.42

Table B.16 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Std. error	Z-score	P-value	Std. estimate
Intercept		PI: 1	0.36	0.11	3.29	0.001	0.77
Intercept		PI: 2	0.38	0.08	4.46	< 0.001	0.79
Intercept		PI: 3	0.22	0.07	3.07	0.002	0.56
Intercept		PI: 4	0.48	0.09	5.47	< 0.001	0.96
Intercept		PI: 5	0.26	0.09	3.00	0.003	0.62
Intercept		PI: 6	0.23	0.08	2.81	0.005	0.57
Intercept		PI: 7	0.30	0.09	3.48	< 0.001	0.68
Intercept		PI: 8	0.08	0.03	2.29	0.022	0.31
Intercept		PI: 9	0.30	0.10	2.91	0.004	0.68
Intercept		PI: 10	0.15	0.07	2.19	0.029	0.46
Intercept		PI: 11	0.32	0.11	2.96	0.003	0.71
Intercept		PI: 12	0.38	0.12	3.18	0.001	0.81
Intercept		PI: 13	0.26	0.08	3.31	0.001	0.62
Intercept		CA	-0.30	0.29	-1.04	0.298	-0.30
Intercept		Friendship support	-0.10	0.28	-0.35	0.727	-0.09
Intercept		Family support	-0.85	0.25	-3.48	0.001	-0.85
Intercept		Age (years)	20.07	0.00	NA	NA	8.05
Intercept		Male	0.47	0.00	NA	NA	0.94
Intercept		Socioeconomic Deprivation (rank)	-0.04	0.00	NA	NA	-0.04
Intercept		Non-white ethnicity	0.23	0.00	NA	NA	0.55
Intercept		Mother's educational qualifications	1.67	0.00	NA	NA	1.51
Intercept		Urban-rural index	5.43	0.00	NA	NA	7.36
Intercept		Family psychiatric history	0.11	0.00	NA	NA	0.35
Intercept		Cannabis use	0.15	0.00	NA	NA	0.42
Intercept		DS	0.00	0.00	NA	NA	0.00
Intercept		AEB	0.00	0.00	NA	NA	0.00
Intercept		PI	0.00	0.00	NA	NA	0.00

Table B.16: Parameter estimates of structural equation model of relationships between childhood adversity, social support and later depressive symptoms and psychotic phenomena fit to NSPN data with a robust maximum-likelihood estimator. Missing data were estimated using full-information maximum likelihood. Parameters with the same Equality constraint label were fixed to be equal. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate.

Appendix C

Psychotic experiences are an index of extreme distress in adolescents and young adults: evidence from two general population samples

C.1 Research questions

- Are self-report PEs a common manifestation of distress, like classical depressive or anxious symptoms, in young people?
- If so, what severity of distress do they indicate?

Abstract

Psychotic experiences (PEs) can be measured by self-report instruments or interview instruments, where the veracity of the PEs is externally assessed. These instruments tend to be developed and applied in different fields; self-report instruments through schizotypy and individual differences frameworks and interview instruments through clinically-oriented psychosis-risk research. It is not known whether self-report and interview instruments measure the same underlying phenomena and whether they measure PEs of the same or different severity/intensity. The convergent validity of different instruments would be supported by showing the same patterns of associations with other variables. Interview-assessed PEs can be modelled as being partly explained by an underlying dimension of common mental distress, which also captures classical depressive symptoms. Interview-assessed PEs have been shown to measure more severe distress than self-report depressive symptoms. In this set of analyses, I tested whether this same pattern can be found for self-report PEs. I attempted to replicate these findings in two large, epidemiologically-principled cohorts of young people with latent variable modelling of self-report state and trait PEs and depressive symptoms. In both cohorts, a bifactor model with a general 'common mental distress' factor explaining some variance in all measured responses and specific factors explaining orthogonal variance in some responses, outperformed models with separate factors or a single factor. Using item response theory, I calculated the severity range of distress measured by each item type and how much information they contributed per item. In one cohort, two trait dimensions of PEs (AEB: anomalous experiences and beliefs; PI: Paranoid ideation) measured more severe

distress than state depressive symptoms, while only state AEB measured more severe distress than state depressive symptoms in the second cohort. PI contributed more information on distress than AEB in both cohorts. These results support that PEs are a transdiagnostic manifestation of severe distress in the general population and support the validity of self-report instruments as measuring similar phenomena to interview assessments.

Psychotic phenomena occurring in the general population are a risk-indicator for psychotic (Fusar-Poli et al., 2013) and non-psychotic (Fusar-Poli et al., 2014) illnesses. Interview-measured psychotic experiences (PEs) and self-report depression-like and anxiety-like symptoms can be well explained by a bifactor latent variable model, in which a general distress factor explains some of the variance in all psychosis and distress items (Stochl et al., 2015). When examined using item response theory analysis, psychotic experiences uniquely measure a more severe range of the general distress factor, not measured by traditional symptoms of depression and anxiety.

In this chapter, I set out to replicate findings that psychotic phenomena are an index of extreme distress in two general population cohorts of adolescents and young adults using self-report measurements of PEs, rather than interview assessments. I generated the following set of analyses to test this hypothesis.

C.1.1 Psychotic phenomena will co-occur with depressive/anxious symptoms

First, I predicted self-report psychotic phenomena would be associated with distress, indicated by correlation between scores on these self-report measures and higher depressive/anxious symptoms in those with interview-verified PEs than those without PEs. People with recent and persistent PEs would experience more depressive/anxious/anxious symptoms than those with non-recent and transient PEs.

C.1.2 A common mental distress factor will underlie psychotic phenomena and depressive/anxious symptoms

Second, I predicted a general factor would explain shared variance in depressive/anxious/anxious symptoms and psychotic phenomena, indicated by a latent bifactor model outperforming unidimensional, correlated-factors and uncorrelated-factors models (Figure C.1) when fit to data on self-report depressive/anxious symptoms and psychosis items. This would be good evidence for a common mental distress factor underlying both psychotic phenomena and depressive/anxious symptoms, suggesting self-report psychotic phenomena are a manifestation of common distress.

C.1.3 Psychosis items will have residual variance that is orthogonal to distress

Thirdly, I predicted there would be additional information explained by a specific factor of psychotic phenomena in the bifactor model. This would be indicated by significant loadings of psychosis items on a specific factor and the ω statistic for that factor, approximating how much of the variance in the items it explains. This would replicate previous findings and suggest that there is covariance among self-report psychosis items that is orthogonal to distress, as was found for interview PEs (Stochl et al., 2015).

C.1.4 Psychosis items will measure a more severe distribution of mental distress than depressive/anxious symptoms

I predicted self-report psychotic phenomena would measure the more extreme distress than classical depressive/anxious symptoms, replicating findings of Stochl et al. (2015). This would be supported firstly by higher

Figure C.1: Family of model structures compared

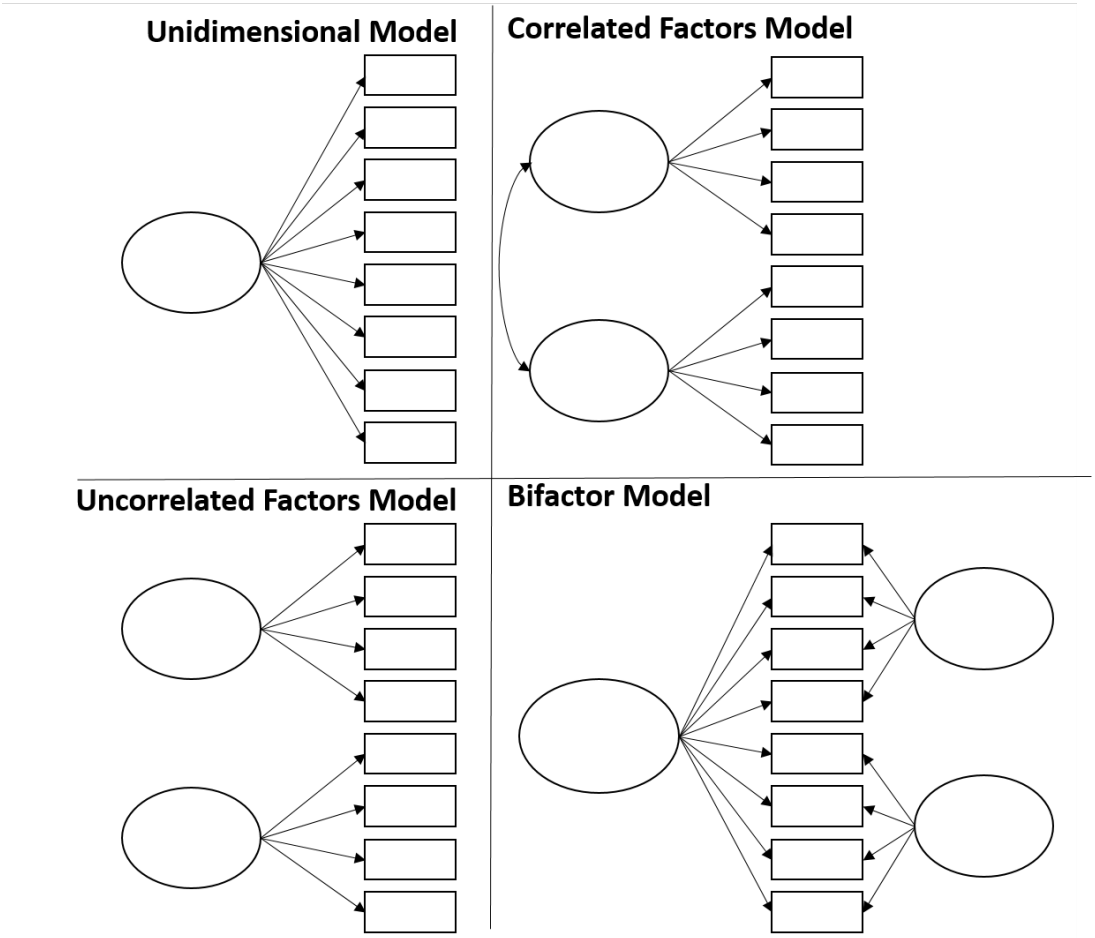

Figure C.1: Diagrams of latent variable model structures. To investigate whether self-report and interview instruments measured the same underlying PEs or distinct constructs, I compared a model with a single factor, two uncorrelated factors, two correlated factors or a bifactor model with a general factor explaining common variance and specific factors explaining residual instrument-specific variance.

thresholds on this factor for psychosis items (the severity of the latent trait at which different categorical responses are emitted). This would also be supported, secondly, by information distributions from unidimensional item response theory (IRT) models (estimations of how precisely an item or group of items measures 'true' scores across the range of severity of the latent trait), fit to the combined psychosis & depressive/anxious symptom items, showing that psychosis items uniquely measure a more severe range of common mental distress. I then attempted to extend the work of Stochl & colleagues with two further analyses. Firstly, I planned to test whether psychosis items or traditional distress items were more informative about common mental distress, on average, by comparing the area under the curve (AUC) of information distributions. Secondly, to understand the implications of a common mental distress factor for traditional sum-score measurements of PEs and depressive symptoms, I quantified the proportion of variance in sum scores on each instrument that is attributable to common mental distress and likely shared with all psychopathology domains, versus specific to domains of psychotic phenomena or depressive symptoms. I estimated scores on the general distress factor and any specific factors, then tested the variance they explain in sum scores (r^2) using a series of linear regressions.

C.2 Methods

C.2.1 Data

Data come from both ROOTS and NSPN. For full information on the cohorts, see Methodology.

C.2.2 Instruments

In ROOTS, self-report psychotic phenomena were measured using the Brief Schizotypal Symptoms Inventory (BSSI), a 20-item self-report instrument measuring psychotic phenomena in the last two weeks. It measures three domains: Anomalous Experiences and Beliefs (AEB), comprising perceptual abnormalities and magical thinking (8 items); Paranoid Ideation (PI), comprising suspiciousness and ideas of reference (6 items, of which one is redundant); and Social Anxiety (SA, 8 items). One item from PI is redundant with another and was removed. The AEB and PI scales measure the same underlying psychosis factor as a semi-structured interview method (Horwood et al., 2008).

Questions were structured as a set of statements or questions. Participants indicated how often that statement applied to them in the last two weeks on a 5-point scale ('Not at all', 'Occasionally', 'Sometimes', 'Often' and 'All the time'.

Due to low endorsement of some categories, in analyses using latent variable modelling, responses were collapsed into a 3-point scale ('Not at all', 'Occasionally', 'Sometimes/Often/All the time'). Collapsing these high-severity responses loses some measurement precision at the more severe ranges of the traits, more so for PI and SA than AEB, but is necessary for model convergence.

In NSPN, self-report psychotic phenomena were measured with the Schizotypal Personality Questionnaire (SPQ), which comprises 74 dichotomous items intended to measure general, trait-like experience of 9 dimensions associated with psychosis-proneness. In Chapter 1, I showed that, while these 9 dimensions are reliable, a number are likely to be redundant. While second-order latent variable models suggest three or four variables explain scores on these subscales, they are not reliable when estimated at the item level. Instead, I identified a reliable 6-factor solution without redundantly high correlations among factors. Of relevance for this study are the dimensions most similar to typical psychotic phenomena: 'Anomalous Experiences & Beliefs' (AEB_{SPQ}), comprising 18 items measuring unusual perceptual experiences and magical thinking and 'Paranoid Ideation' (PI_{SPQ}), comprising 13 items measuring suspiciousness and ideas of reference.

In both cohorts, self-report depressive/anxious symptoms were measured with the Mood and Feelings Questionnaire (MFQ) (Costello and Angold, 1988). The full questionnaire comprises 33 items on common symptoms of depression and anxiety occurring over the last two weeks. The full MFQ is likely to be multidimensional (Brodbeck et al., 2011) and has more items than the AEB and PI scales of both the SPQ and SSI, which may

pull any common factors estimated from combined psychosis and distress items towards measuring traditional distress and result in numerous specific factors. I therefore used the items that comprise the Short Mood and Feelings Questionnaire (SMFQ) (Angold et al., 1995), which are contained within the full MFQ. These items were used previously in identifying a common factor underlying mood, anxiety and psychotic experiences (Stochl et al., 2015). The SMFQ is likely to be unidimensional and is able to predict clinical depression and anxiety with reasonable sensitivity (Turner et al., 2014).

In ROOTS, I combined all 8 items from the AEB_{BSSI} scale and 5 of the 6 items from the PI_{BSSI} scale with the 13 SMFQ items, creating a pool of 26 psychosis-distress items.

In NSPN, the SPQ items were dichotomous and more numerous than the SMFQ items, with 18 items on the AEB_{SPQ} scale and 13 on the PI_{SPQ} scale. Polychoric correlations account for the differences in item response levels. Data from 44 items were entered into latent variable modelling.

C.2.3 Statistical analyses

Due to highly skewed distributions of total scores on distress and psychotic phenomena, I used non-parametric Spearman's rank correlations and partial correlations to compare scores on self-report distress and psychotic phenomena. To compare distress in groups of participants with different verified PEs, I used Wilcoxon rank-sum tests.

To test the latent model structure that best explains psychosis-proneness and distress items, I fit a number of latent variable models to the combined items using a full-information robust maximum likelihood estimator (MLR), with missing data patterns estimated using maximum likelihood. This generated comparative fit indices AIC, BIC and SABIC. The model with the lowest value on these indices was the winner.

I compared four families of model structures: unidimensional, correlated-factors, uncorrelated-factors and bifactor models (Figure C.1). Briefly, in unidimensional models, all items are explained by a single latent variable. In correlated-factors models, there is a latent variable for each scale type that are allowed to correlate. In uncorrelated-factors models, there is a latent variable for each scale type and the latent variables are constrained to be orthogonal. In a bifactor model, there is a single general factor explaining common variance among all items and a number of specific factors explaining variance in smaller groups of items. The general and all specific factors are constrained to be orthogonal to ensure identifiability.

I estimated two bifactor models with different structures of specific factors (Bifactor A: One specific factor for SMFQ items, one for AEB items, one for PI items; Bifactor B: One specific factor for SMFQ items, one for AEB & PI items).

Provided good fit of the MLR-estimated bifactor model, I approximated how much of the variance in the items is explained by each latent factor and how much is attributable to error by calculating Omega values.

To test the information distributions of psychosis and distress items, I fit unidimensional two-parameter logistic (2PL) item response theory (IRT) to all items, approximating the general factor. To account for non-normality of the latent trait distribution, I estimated IRT solutions with the conventional assumption of a normal latent trait distribution and with a prior on the trait distribution empirically estimated using histograms of item scores, allowing for non-normality. I calculated information values for each item across a broad severity range of the latent trait measured. Information is additive, so I calculated the mean information contributed for each scale at each location on the trait distribution and compared the distributions for each scale. I also calculated information contributed by taking the area under the curve (AUC) of each item and compared these across scales using Wilcoxon rank-sum tests.

To quantify variance in traditional sum scores explained by latent factors, I estimated factor scores from the winning model using an empirical Bayes modal method that allowed for non-normality of latent variable distributions. I then regressed these factor scores on to sum scores, individually then in conjunction, and reported the r^2 statistic for each one.

Table C.1: Results of comparison of different model structures fit to combined self-report PEs and depressive symptoms in ROOTS

Model	AIC	BIC	SABIC
Unidimensional	37310.26491	37690.12907	37442.4027
Two Correlated Factors	36096.37553	36481.10975	36230.20739
Two Uncorrelated Factors	36413.66505	36793.52922	36545.80285
Three Correlated Factors	35275.83825	35670.31258	35413.05827
Three Uncorrelated Factors	35745.47311	36125.33727	35877.6109
Bifactor A	34973.5029	35479.98845	35149.68662
Bifactor B	35090.18551	35596.67107	35266.36924

Table C.1: Results of model comparison of competing structures fit to self-report and interview PEs data in ROOTS using fit indices that trade-off model fit with model parsimony. Lower values indicate better fit. The winning model was Bifactor A.

C.3 Results

C.3.1 Results I: ROOTS

Data

1074 ROOTS participants took part at the third assessment (when aged 17).

1056 participants completed the PLIKSi. 939 had complete data on the AEB_{BSSI} scale and 950 had complete data on the PI_{BSSI} scale. 997 had complete data on the SMFQ items.

914 people had fully complete data on the AEB_{BSSI}, PI_{BSSI} and SMFQ scales.

Psychotic phenomena co-occur with distress

Total scores on the SMFQ rank-correlated with AEB_{BSSI} (rho = 0.32, $p < 0.0001$), and PI_{BSSI} (rho = 0.55, $p < 0.0001$).

Paranoid ideation and distress appeared to overlap more so than distress and anomalous experiences and beliefs. On partial correlations, AEB_{BSSI} showed a small but significant rank-correlation with SMFQ, controlling for PI_{BSSI} (partial rho = 0.11, p = 0.0003). PI_{BSSI} showed a large partial rank-correlation with SMFQ, controlling for AEB_{BSSI} (partial rho = 0.47, $p < 0.0001$).

A common distress factor underlies psychotic phenomena and traditional symptoms of distress

Table C.1 shows the comparative fit indices of the MLR-estimated latent variable models.

The winning model was Bifactor A, with a general factor and three specific factors each explaining residual variance in items from the SMFQ, AEB_{BSSI} or PI_{BSSI} scales.

However, when this model was fit to the data using a WLSMV estimator, one of the items was estimated with a negative residual variance, making the model results inadmissible. This issue also occurred for this item when

fitting a bifactor model to combined verified and self-report psychosis items using this scale in Chapter 6 (main text).

The second best-fitting MLR-estimated model was Bifactor B, with a general factor, one specific factor explaining residual variance in the SMFQ items and one specific factor explaining residual variance in the combined AEB_{BSSI} and PI_{BSSI} items. This model also performed well on other fit indices (CFI = 0.918, TLI = 0.902, RMSEA = 0.045). All of the loadings on the specific factor of SMFQ items were positive and significant. 4 of the 13 loadings of PI items on the specific factor of AEB_{BSSI} and PI_{BSSI} items were negative and non-significant.

Table C.2: Parameter estimates from combined SMFQ and BSSI items in ROOTS (WLSMV, 25 imputed datasets)

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	GF	AEB: 2	1	0	NA	NA	0.45
Loading	GF	AEB: 5	1.24	0.12	10.01	0	0.57
Loading	GF	AEB: 8	1.09	0.11	9.55	0	0.51
Loading	GF	AEB: 10	1.11	0.15	7.64	0	0.52
Loading	GF	AEB: 13	1.32	0.14	9.45	0	0.61
Loading	GF	AEB: 16	1.09	0.12	8.92	0	0.5
Loading	GF	AEB: 18	0.98	0.07	13.41	0	0.44
Loading	GF	AEB: 20	1.02	0.13	8.18	0	0.47
Loading	GF	PI: 3	1.69	0.21	7.9	0	0.79
Loading	GF	PI: 9	1.65	0.22	7.4	0	0.77
Loading	GF	PI: 12	1.69	0.22	7.81	0	0.79
Loading	GF	PI: 15	1.87	0.25	7.49	0	0.87
Loading	GF	PI: 19	1.49	0.16	9.23	0	0.7
Loading	GF	SMFQ: 1	0.88	0.13	6.99	0	0.41
Loading	GF	SMFQ: 2	1	0.14	7.24	0	0.47
Loading	GF	SMFQ: 3	0.7	0.11	6.34	0	0.33
Loading	GF	SMFQ: 4	0.74	0.12	6.35	0	0.35
Loading	GF	SMFQ: 5	0.95	0.13	7.04	0	0.44
Loading	GF	SMFQ: 6	0.82	0.12	6.94	0	0.39
Loading	GF	SMFQ: 7	0.9	0.13	6.91	0	0.42
Loading	GF	SMFQ: 8	1.16	0.15	7.6	0	0.54
Loading	GF	SMFQ: 9	1.02	0.14	7.09	0	0.48
Loading	GF	SMFQ: 10	1.1	0.15	7.47	0	0.51
Loading	GF	SMFQ: 11	1.16	0.16	7.4	0	0.54
Loading	GF	SMFQ: 12	1.02	0.14	7.1	0	0.48
Loading	GF	SMFQ: 13	1.02	0.15	6.99	0	0.48
Loading	SF1	AEB: 2	1	0	NA	NA	0.12
Loading	SF1	AEB: 5	2.09	0.99	2.12	0.03	0.25
Loading	SF1	AEB: 8	1.01	0.55	1.81	0.07	0.12

Table C.2 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	SF1	AEB: 10	2.74	1.19	2.31	0.02	0.33
Loading	SF1	AEB: 13	-1.42	1.16	-1.23	0.22	-0.17
Loading	SF1	AEB: 16	-6.22	3.67	-1.7	0.09	-0.73
Loading	SF1	AEB: 18	-3.66	2.35	-1.55	0.12	-0.44
Loading	SF1	AEB: 20	-3.88	2.39	-1.62	0.1	-0.47
Loading	SF1	PI: 3	-2.04	1.45	-1.41	0.16	-0.25
Loading	SF1	PI: 9	-3.29	2.15	-1.53	0.13	-0.4
Loading	SF1	PI: 12	-4.04	2.51	-1.61	0.11	-0.48
Loading	SF1	PI: 15	-6.3	3.74	-1.68	0.09	-0.74
Loading	SF1	PI: 19	-5.43	3.22	-1.69	0.09	-0.64
Loading	SF2	SMFQ: 1	1	0	NA	NA	0.63
Loading	SF2	SMFQ: 2	0.82	0.07	11.74	0	0.51
Loading	SF2	SMFQ: 3	0.55	0.07	8.46	0	0.35
Loading	SF2	SMFQ: 4	0.48	0.07	7.1	0	0.3
Loading	SF2	SMFQ: 5	1.14	0.07	15.24	0	0.72
Loading	SF2	SMFQ: 6	0.86	0.07	12.87	0	0.54
Loading	SF2	SMFQ: 7	0.82	0.07	12.06	0	0.52
Loading	SF2	SMFQ: 8	1.07	0.07	16.02	0	0.67
Loading	SF2	SMFQ: 9	0.8	0.08	10.05	0	0.5
Loading	SF2	SMFQ: 10	0.89	0.06	14.46	0	0.56
Loading	SF2	SMFQ: 11	0.97	0.07	13.09	0	0.61
Loading	SF2	SMFQ: 12	0.85	0.07	11.68	0	0.54
Loading	SF2	SMFQ: 13	1	0.08	13.22	0	0.63
Covariance	General Factor	SF1	0	0	NA	NA	0
Covariance	General Factor	SF2	0	0	NA	NA	0
Covariance	SF1	SF2	0	0	NA	NA	0
Threshold	0->1	AEB: 2	0.58	0.04	14	0	0.56
Threshold	1->2	AEB: 2	1.15	0.05	23.24	0	1.12
Threshold	0->1	AEB: 5	0.67	0.04	15.08	0	0.66
Threshold	1->2	AEB: 5	1.26	0.06	21.92	0	1.24
Threshold	0->1	AEB: 8	0.96	0.05	20.94	0	0.94
Threshold	1->2	AEB: 8	1.5	0.06	24.14	0	1.48
Threshold	0->1	AEB: 10	1.06	0.05	22.09	0	1.05
Threshold	1->2	AEB: 10	1.49	0.06	23.53	0	1.48
Threshold	0->1	AEB: 13	1.34	0.06	22.14	0	1.33

Table C.2 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Threshold	1->2	AEB: 13	1.95	0.09	21.54	0	1.93
Threshold	0->1	AEB: 16	1.19	0.05	21.93	0	1.18
Threshold	1->2	AEB: 16	1.89	0.08	24.69	0	1.86
Threshold	0->1	AEB: 18	0.62	0.04	15.24	0	0.6
Threshold	1->2	AEB: 18	1.22	0.05	23.43	0	1.18
Threshold	0->1	AEB: 20	1.49	0.06	24.03	0	1.45
Threshold	1->2	AEB: 20	2.01	0.09	23.13	0	1.96
Threshold	0->1	PI: 3	-0.33	0.04	-8.19	0	-0.33
Threshold	1->2	PI: 3	0.78	0.04	17.73	0	0.78
Threshold	0->1	PI: 9	0.2	0.04	4.73	0	0.2
Threshold	1->2	PI: 9	1.11	0.05	23.2	0	1.11
Threshold	0->1	PI: 12	0.69	0.05	14.83	0	0.68
Threshold	1->2	PI: 12	1.43	0.06	23.68	0	1.43
Threshold	0->1	PI: 15	-0.05	0.04	-1.36	0.17	-0.05
Threshold	1->2	PI: 15	1.01	0.05	21.25	0	1.01
Threshold	0->1	PI: 19	0.32	0.04	7.58	0	0.32
Threshold	1->2	PI: 19	1.17	0.05	22.77	0	1.16
Threshold	0->1	SMFQ: 1	-0.63	0.04	-15.42	0	-0.63
Threshold	1->2	SMFQ: 1	1.52	0.06	24.92	0	1.52
Threshold	0->1	SMFQ: 2	0.33	0.04	8.09	0	0.33
Threshold	1->2	SMFQ: 2	1.95	0.08	24.91	0	1.94
Threshold	0->1	SMFQ: 3	-0.47	0.04	-11.7	0	-0.46
Threshold	1->2	SMFQ: 3	1.05	0.05	22.21	0	1.05
Threshold	0->1	SMFQ: 4	-0.07	0.04	-1.73	0.08	-0.07
Threshold	1->2	SMFQ: 4	1.25	0.05	24.26	0	1.25
Threshold	0->1	SMFQ: 5	0.66	0.04	15.5	0	0.66
Threshold	1->2	SMFQ: 5	1.75	0.07	26.31	0	1.75
Threshold	0->1	SMFQ: 6	0.61	0.04	14.18	0	0.61
Threshold	1->2	SMFQ: 6	1.63	0.06	26.27	0	1.63
Threshold	0->1	SMFQ: 7	-0.35	0.04	-8.63	0	-0.35
Threshold	1->2	SMFQ: 7	1.22	0.05	23.82	0	1.22
Threshold	0->1	SMFQ: 8	0.97	0.05	20.42	0	0.97
Threshold	1->2	SMFQ: 8	1.83	0.07	25.64	0	1.83
Threshold	0->1	SMFQ: 9	1	0.05	20.84	0	0.99
Threshold	1->2	SMFQ: 9	2.23	0.1	22.54	0	2.23
Threshold	0->1	SMFQ: 10	0.29	0.04	7.09	0	0.29
Threshold	1->2	SMFQ: 10	1.42	0.06	24.65	0	1.42

Table C.2 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Threshold	0->1	SMFQ: 11	1.07	0.05	22.65	0	1.07
Threshold	1->2	SMFQ: 11	1.8	0.07	25.36	0	1.8
Threshold	0->1	SMFQ: 12	0.5	0.04	12.09	0	0.5
Threshold	1->2	SMFQ: 12	1.55	0.06	25.44	0	1.55
Threshold	0->1	SMFQ: 13	0.73	0.04	17.24	0	0.73
Threshold	1->2	SMFQ: 13	1.93	0.08	25.37	0	1.93
Residual		AEB: 2	0.27	0.02	14.02	0	0.26
Residual		AEB: 5	0.49	0.02	21.96	0	0.48
Residual		AEB: 8	0.54	0.02	27.07	0	0.53
Residual		AEB: 10	0.68	0.02	42.63	0	0.67
Residual		AEB: 13	0.48	0.03	18.16	0	0.47
Residual		AEB: 16	0.53	0.03	15.4	0	0.51
Residual		AEB: 18	0.27	0.02	13.2	0	0.25
Residual		AEB: 20	0.38	0.03	13.67	0	0.37
Residual		PI: 3	0.36	0.01	27.36	0	0.36
Residual		PI: 9	0.35	0.02	20.58	0	0.34
Residual		PI: 12	0.36	0.02	23.82	0	0.36
Residual		PI: 15	0.13	0.01	11.57	0	0.13
Residual		PI: 19	0.49	0.01	33.21	0	0.49
Residual		SMFQ: 1	0.44	0.02	19.62	0	0.44
Residual		SMFQ: 2	0.52	0.01	41.87	0	0.52
Residual		SMFQ: 3	0.77	0.01	92.21	0	0.77
Residual		SMFQ: 4	0.79	0.01	96.04	0	0.79
Residual		SMFQ: 5	0.29	0.02	12.78	0	0.29
Residual		SMFQ: 6	0.56	0.02	32.81	0	0.56
Residual		SMFQ: 7	0.56	0.01	41.29	0	0.56
Residual		SMFQ: 8	0.25	0.02	12.87	0	0.25
Residual		SMFQ: 9	0.52	0.01	42.95	0	0.52
Residual		SMFQ: 10	0.42	0.01	35.5	0	0.42
Residual		SMFQ: 11	0.34	0.02	17.3	0	0.34
Residual		SMFQ: 12	0.48	0.01	34.06	0	0.48
Residual		SMFQ: 13	0.38	0.01	40.1	0	0.38
Variance		General Factor	0.22	0.05	4.31	0	1
Variance		SF1	0.01	0.01	1.08	0.28	1
Variance		SF2	0.39	0.04	9.46	0	1

Table C.2 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate

Table C.2: Parameter estimates from bifactor model fit to combined SMFQ and BSSI items with a robust weighted-least-squares (WLSMV) estimator to 25 imputed data sets in ROOTS. GF = general factor. SF1 = specific BSSI factor. SF2 = specific SMFQ factor. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate.

This model fit the data from 25 imputed datasets excellently when fit with a WLSMV estimator (CFI = 0.977, TLI = 0.971, RMSEA = 0.039). There were no negative residual item variances. Table C.2) shows the parameter estimates from this model fit to imputed datasets.

The general distress factor explains the majority of the variance in psychosis and distress items

I calculated ω statistics from the MLR-estimated model. This statistic cannot be estimated from factors with negative loadings. I therefore re-estimated a factor model, deleting all negative-loading items from the AEB_{BSSI}/PI_{BSSI} specific factor.

The general factor explained 64.6% of the item variance. The specific factor of SMFQ items explained 18.9% of the variance. The specific factor of AEB_{BSSI}/PI_{BSSI} items explained 8.3% of the variance. 8.1% of the item variance was residual error.

Anomalous experiences and beliefs measure more severe common mental distress than paranoia and traditional depressive/anxious and anxious symptoms

SMFQ and PI_{BSSI} items measured similar severity ranges of mental distress, shown by mostly overlapping information distributions, whether the latent trait was estimated assuming a Gaussian distribution or empirically constructing a prior on the shape of the distribution (see Figure C.2). AEB_{BSSI} items measured a more severe range of mental distress, indicated by these items uniquely contributing information to the higher end of the distress trait. This replicates previous findings with interview psychotic experiences and confirms that, when covarying with other markers of distress, anomalous experiences and beliefs indicate the most severe distress.

SMFQ items contributed more information to the distress factor, on average, than AEB items, indicated by higher AUC for the information distributions of SMFQ items than AEB items, revealed with Wilcoxon rank-sum test (SMFQ: mean AUC = 3.32, SD = 0.96; AEB_{BSSI}: mean AUC = 1.38, SD = 0.32; W = 102, $p < 0.0001$). PI items also contributed more information to the distress factor than AEB items (PI: mean AUC = 2.67, SD = 0.43; W = 40, p = 0.002). The average information contributed by SMFQ and PI items did not significantly differ.

Variance in sum scores attributable to general distress and specific factors

See Table C.3 for full results of linear regressions on sum scores.

35.0% of the variance in AEB scores was explained by the general distress factor, while the specific factor of SMFQ items explained a negligible amount and the specific factor of PE items explained 49.7%. Together, the distress factor and the specific PEs factor explained 85.0% of the variance.

Figure C.2 Information distributions of self-report PEs and depressive symptoms in ROOTS

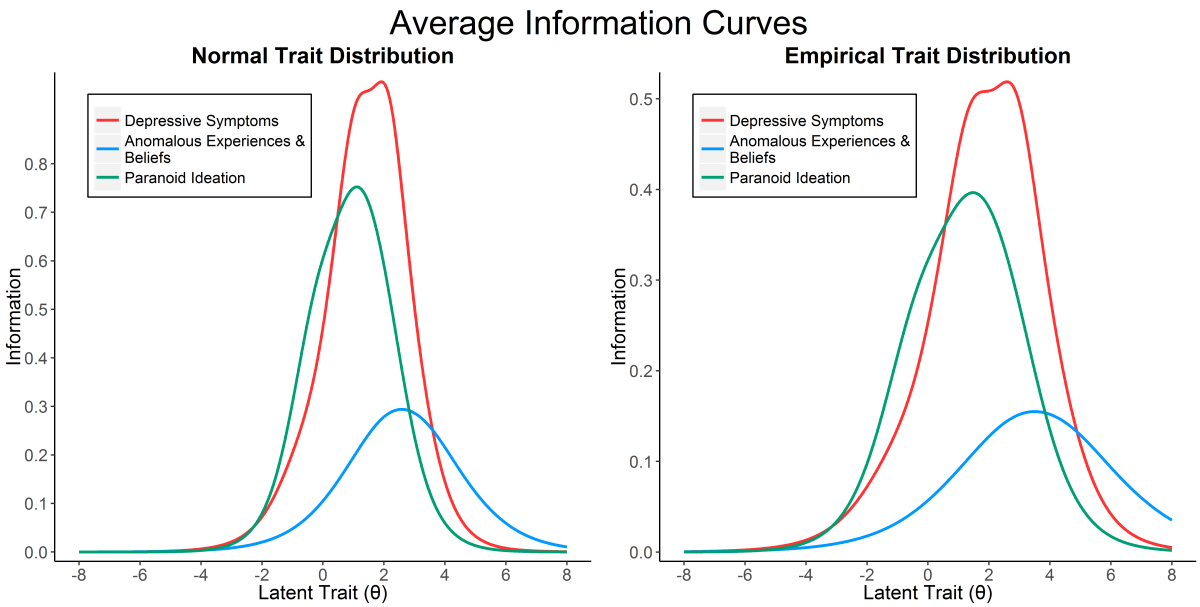

Figure C.2: Information distributions were estimated using parametric item response theory analyses with two-parameter logistic curves. The curves quantify where along the distribution of a latent trait an item contributes information and thus is able to measure common mental distress. Anomalous Experiences & Beliefs uniquely measured a slightly more severe range of distress than Paranoid Ideation or depressive symptoms. The distributions were very similar for both traits assumed to have a normal distribution and empirically-estimated distributions.

Table C.3: Proportion of variance in sum-scores on self-report PEs and depressive symptoms that is explained by the general and specific factors from the bifactor model in ROOTS.

Factor	AEB_{BSSI}	PI_{BSSI}	SMFQ
GF	0.35	0.907	0.388
SF1 (SMFQ)	0	0.002	0.653
SF2 (PE)	0.497	0.019	0
GF + SF1 (SMFQ)	0.356	0.916	0.918
GF + SF2 (PE)	0.85	0.929	0.388
All factors	0.853	0.939	0.918

Table C.3: AEB = Anomalous Experiences & Beliefs, PI = Paranoid Ideation, SMFQ = Short Mood and Feelings Questionnaire. BSSI = Brief Schizotypal Symptoms Inventory.

Table C.4: Results of comparison of different model structures fit to combined self-report PEs and depressive symptoms in NSPN

Model	AIC	BIC	SABIC
Unidimensional	112053.9467	112816.6153	112397.2228
Two Correlated Factors	107607.6349	108376.0813	107953.5115
Three Correlated Factors	105580.1949	106360.197	105931.2728
Two Uncorrelated Factors	108402.673	109165.3416	108745.9491
Three Uncorrelated Factors	107240.675	108003.3437	107583.9511
"Bifactor (Sp. SMFQ, Sp. AEB, Sp. PI)"	104430.6377	105447.5292	104888.3391
"Bifactor (Sp. SMFQ, SP. AEB & PI)"	104886.6925	105903.584	105344.3939
"Bifactor (Sp. SMFQ, Sp. AEB)"	105112.1702	106053.9504	105536.0642

Table C.4: Results of model comparison of competing structures fit to self-report and interview PEs data in NSPN using fit indices that trade-off model fit with model parsimony. Lower values indicate better fit. The winning model was Bifactor (Sp. SMFQ, Sp. AEB, Sp. PI).

90.7% of the variance in PI was explained by the general distress factor. The specific factors of SMFQ and PEs each explained less than 2% of the variance. This suggests that paranoia always tends to manifest in conjunction with distress.

38.8% of the variance in depressive symptoms were explained by the general distress factor. The specific factor of SMFQ Items explained 65.3% of the variance, while the specific PEs factor explained none. Together, the general factor and specific SMFQ factors explained 91.8% of the variance.

C.3.2 Results II: NSPN

Data

2388 participants returned questionnaire packs at baseline, as of July 2016. 2322 had complete data on all SMFQ items, 2287 had complete data on all AEB_{SPQ} items and 2290 had complete data on all PI_{SPQ} items. 2170 participants had complete data on the SMFQ, AEB_{SPQ} and PI_{SPQ}.

Psychotic phenomena co-occur with distress

Total scores on the SMFQ rank-correlated with AEB_{SPQ} (rho = 0.38, $p < 0.0001$), and PI_{SPQ} (rho = 0.54, $p < 0.0001$).

Paranoid ideation and distress appeared to overlap more so than distress and anomalous experiences and beliefs. On partial correlations, AEB_{SPQ} showed a small but significant rank-correlation with SMFQ, controlling for PI_{SPQ} (partial rho = 0.11, $p < 0.0001$). PI_{SPQ} showed a larger partial rank-correlation with SMFQ, controlling for AEB_{SPQ} (partial rho = 0.42, $p < 0.0001$).

A common distress factor underlies psychotic phenomena and depressive/anxious symptoms

Table C.4 shows the comparative fit indices of the MLR-estimated latent variable models.

The winning model was Bifactor (Sp. SMFQ, Sp. AEB, Sp. PI), with a general factor and three specific factors each explaining residual variance in items from the SMFQ, AEB_{SPQ} or PI_{SPQ} scales. This model also performed well on RMSEA but fell short of acceptable fit on CFI and TLI (CFI = 0.895, TLI = 0.884, RMSEA = 0.035). All of the loadings on the general factor and the specific factors of SMFQ and AEB items were positive and significant. 9 of the 13 item loadings on the specific PI factor were positive and significant; the rest were non-significant, for 1 of which the loading was negative.

Table C.5: Parameter estimates from bifactor SMFQ & SPQ model in NSPN (WLSMV, 25 imputed datasets)

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	GF	SMFQ: 1	1	0	NA	NA	0.46
Loading	GF	SMFQ: 2	0.97	0.05	17.78	0	0.44
Loading	GF	SMFQ: 3	0.84	0.06	14.61	0	0.38
Loading	GF	SMFQ: 4	0.76	0.06	13.23	0	0.35
Loading	GF	SMFQ: 5	1.14	0.06	19.46	0	0.52
Loading	GF	SMFQ: 6	0.88	0.06	14.11	0	0.4
Loading	GF	SMFQ: 7	1.01	0.06	18.04	0	0.46
Loading	GF	SMFQ: 8	1.22	0.06	19.92	0	0.56
Loading	GF	SMFQ: 9	1.21	0.07	17.51	0	0.55
Loading	GF	SMFQ: 10	1.04	0.05	19.02	0	0.47
Loading	GF	SMFQ: 11	1.26	0.07	18.88	0	0.57
Loading	GF	SMFQ: 12	1.15	0.06	18.68	0	0.52
Loading	GF	SMFQ: 13	1.28	0.07	18.39	0	0.58
Loading	GF	AEB: 1	0.67	0.07	9.69	0	0.3
Loading	GF	AEB: 3	0.7	0.08	8.4	0	0.32
Loading	GF	AEB: 4	1.13	0.07	15.36	0	0.52
Loading	GF	AEB: 12	0.68	0.08	8.32	0	0.31
Loading	GF	AEB: 13	1.02	0.08	13.55	0	0.47
Loading	GF	AEB: 21	1.11	0.08	13.92	0	0.51
Loading	GF	AEB: 22	1.09	0.1	10.78	0	0.5
Loading	GF	AEB: 28	1.03	0.08	13.08	0	0.47
Loading	GF	AEB: 30	0.62	0.08	7.74	0	0.28
Loading	GF	AEB: 31	1.04	0.08	12.6	0	0.48
Loading	GF	AEB: 37	1.03	0.08	12.3	0	0.47
Loading	GF	AEB: 39	0.96	0.1	9.85	0	0.44
Loading	GF	AEB: 40	1.14	0.09	12.24	0	0.52
Loading	GF	AEB: 47	0.79	0.09	8.8	0	0.36
Loading	GF	AEB: 55	0.95	0.1	9.75	0	0.43
Loading	GF	AEB: 56	0.92	0.08	12.06	0	0.42
Loading	GF	AEB: 61	1.3	0.08	16.13	0	0.6

Table C.5 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	GF	AEB: 64	1.31	0.08	16.27	0	0.6
Loading	GF	PI: 9	1.64	0.09	17.4	0	0.75
Loading	GF	PI: 10	1.11	0.08	13.45	0	0.51
Loading	GF	PI: 19	1.54	0.09	17.31	0	0.71
Loading	GF	PI: 27	1.51	0.09	17.08	0	0.69
Loading	GF	PI: 36	1.71	0.1	17.82	0	0.78
Loading	GF	PI: 44	1.56	0.09	16.98	0	0.72
Loading	GF	PI: 45	1.34	0.09	15.34	0	0.61
Loading	GF	PI: 48	1.59	0.1	15.98	0	0.73
Loading	GF	PI: 53	1.48	0.09	16.04	0	0.68
Loading	GF	PI: 59	1.82	0.1	17.65	0	0.83
Loading	GF	PI: 60	1.6	0.09	17.2	0	0.73
Loading	GF	PI: 63	1.58	0.1	16.17	0	0.72
Loading	GF	PI: 65	1.5	0.09	16.69	0	0.68
Loading	SF1	SMFQ: 1	1	0	NA	NA	0.61
Loading	SF1	SMFQ: 2	0.84	0.04	20.37	0	0.51
Loading	SF1	SMFQ: 3	0.58	0.04	13.44	0	0.35
Loading	SF1	SMFQ: 4	0.51	0.04	11.59	0	0.31
Loading	SF1	SMFQ: 5	1.12	0.04	25.68	0	0.68
Loading	SF1	SMFQ: 6	0.78	0.05	16.5	0	0.48
Loading	SF1	SMFQ: 7	0.9	0.04	21.28	0	0.55
Loading	SF1	SMFQ: 8	1.1	0.04	25.5	0	0.67
Loading	SF1	SMFQ: 9	0.79	0.05	17.35	0	0.48
Loading	SF1	SMFQ: 10	0.98	0.04	23.67	0	0.6
Loading	SF1	SMFQ: 11	1	0.05	21.72	0	0.61
Loading	SF1	SMFQ: 12	0.96	0.04	22.13	0	0.58
Loading	SF1	SMFQ: 13	0.94	0.04	21.21	0	0.57
Loading	SF2	AEB: 1	1	0	NA	NA	0.31
Loading	SF2	AEB: 3	2.08	0.24	8.52	0	0.64
Loading	SF2	AEB: 4	0.81	0.13	6.38	0	0.25
Loading	SF2	AEB: 12	2.31	0.25	9.08	0	0.71
Loading	SF2	AEB: 13	1.84	0.21	8.64	0	0.57
Loading	SF2	AEB: 21	0.99	0.15	6.79	0	0.3
Loading	SF2	AEB: 22	1.24	0.18	6.78	0	0.38
Loading	SF2	AEB: 28	1.67	0.19	8.92	0	0.51
Loading	SF2	AEB: 30	2.34	0.27	8.76	0	0.72
Loading	SF2	AEB: 31	1.14	0.17	6.71	0	0.35

Table C.5 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Loading	SF2	AEB: 37	1.6	0.18	8.69	0	0.49
Loading	SF2	AEB: 39	1.46	0.2	7.19	0	0.45
Loading	SF2	AEB: 40	1.88	0.24	7.9	0	0.58
Loading	SF2	AEB: 47	2.09	0.24	8.59	0	0.64
Loading	SF2	AEB: 55	1.86	0.23	8.14	0	0.57
Loading	SF2	AEB: 56	1.25	0.17	7.32	0	0.39
Loading	SF2	AEB: 61	1.1	0.15	7.34	0	0.34
Loading	SF2	AEB: 64	1.3	0.17	7.64	0	0.4
Loading	SF3	PI: 9	1	0	NA	NA	0.25
Loading	SF3	PI: 10	1.85	0.29	6.34	0	0.46
Loading	SF3	PI: 19	0.03	0.16	0.2	0.84	0.01
Loading	SF3	PI: 27	0.22	0.15	1.45	0.15	0.06
Loading	SF3	PI: 36	-0.28	0.19	-1.49	0.14	-0.07
Loading	SF3	PI: 44	-0.09	0.17	-0.56	0.58	-0.02
Loading	SF3	PI: 45	1.85	0.28	6.58	0	0.46
Loading	SF3	PI: 48	-0.74	0.26	-2.85	0	-0.19
Loading	SF3	PI: 53	1.93	0.26	7.43	0	0.48
Loading	SF3	PI: 59	0.5	0.15	3.21	0	0.12
Loading	SF3	PI: 60	1.03	0.17	5.99	0	0.26
Loading	SF3	PI: 63	2.34	0.31	7.6	0	0.58
Loading	SF3	PI: 65	-0.22	0.18	-1.2	0.23	-0.06
Loading	General Factor	SF1	0	0	NA	NA	0
Loading	General Factor	SF2	0	0	NA	NA	0
Loading	General Factor	SF3	0	0	NA	NA	0
Loading	SF1	SF2	0	0	NA	NA	0
Loading	SF1	SF3	0	0	NA	NA	0
Loading	SF2	SF3	0	0	NA	NA	0
Threshold	0->1	SMFQ: 1	-0.84	0.03	-28.76	0	-0.84
Threshold	1->2	SMFQ: 1	1.27	0.03	36.48	0	1.27
Threshold	0->1	SMFQ: 2	0.19	0.03	7.46	0	0.19
Threshold	1->2	SMFQ: 2	1.66	0.04	37.96	0	1.66
Threshold	0->1	SMFQ: 3	-0.51	0.03	-18.81	0	-0.51
Threshold	1->2	SMFQ: 3	0.86	0.03	29.18	0	0.86
Threshold	0->1	SMFQ: 4	-0.18	0.03	-7.14	0	-0.18
Threshold	1->2	SMFQ: 4	1.06	0.03	33.41	0	1.06

Table C.5 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Threshold	0->1	SMFQ: 5	0.38	0.03	14.47	0	0.38
Threshold	1->2	SMFQ: 5	1.32	0.04	37	0	1.32
Threshold	0->1	SMFQ: 6	0.65	0.03	23.49	0	0.65
Threshold	1->2	SMFQ: 6	1.55	0.04	38.08	0	1.55
Threshold	0->1	SMFQ: 7	-0.53	0.03	-19.51	0	-0.53
Threshold	1->2	SMFQ: 7	0.9	0.03	30.09	0	0.9
Threshold	0->1	SMFQ: 8	0.56	0.03	20.54	0	0.56
Threshold	1->2	SMFQ: 8	1.39	0.04	37.52	0	1.39
Threshold	0->1	SMFQ: 9	0.52	0.03	19.23	0	0.52
Threshold	1->2	SMFQ: 9	1.68	0.04	37.94	0	1.68
Threshold	0->1	SMFQ: 10	-0.13	0.03	-4.87	0	-0.13
Threshold	1->2	SMFQ: 10	0.98	0.03	31.94	0	0.98
Threshold	0->1	SMFQ: 11	0.72	0.03	25.37	0	0.72
Threshold	1->2	SMFQ: 11	1.42	0.04	37.68	0	1.42
Threshold	0->1	SMFQ: 12	0.11	0.03	4.1	0	0.11
Threshold	1->2	SMFQ: 12	1	0.03	32.38	0	1
Threshold	0->1	SMFQ: 13	0.5	0.03	18.52	0	0.5
Threshold	1->2	SMFQ: 13	1.51	0.04	37.99	0	1.51
Threshold	0->1	AEB: 1	0.24	0.03	9.33	0	0.24
Threshold	0->1	AEB: 3	1.12	0.03	34.42	0	1.12
Threshold	0->1	AEB: 4	0.15	0.03	5.76	0	0.15
Threshold	0->1	AEB: 12	1.11	0.03	34.15	0	1.11
Threshold	0->1	AEB: 13	0.51	0.03	18.91	0	0.51
Threshold	0->1	AEB: 21	0.77	0.03	26.95	0	0.77
Threshold	0->1	AEB: 22	1.49	0.04	37.95	0	1.49
Threshold	0->1	AEB: 28	0.81	0.03	27.95	0	0.81
Threshold	0->1	AEB: 30	1.02	0.03	32.56	0	1.02
Threshold	0->1	AEB: 31	0.99	0.03	32.11	0	0.99
Threshold	0->1	AEB: 37	1.17	0.03	35.2	0	1.17
Threshold	0->1	AEB: 39	1.5	0.04	37.89	0	1.5
Threshold	0->1	AEB: 40	1.4	0.04	37.45	0	1.4
Threshold	0->1	AEB: 47	1.33	0.04	36.93	0	1.33
Threshold	0->1	AEB: 55	1.45	0.04	37.81	0	1.45
Threshold	0->1	AEB: 56	0.79	0.03	27.28	0	0.79
Threshold	0->1	AEB: 61	0.49	0.03	18.39	0	0.49
Threshold	0->1	AEB: 64	0.66	0.03	23.64	0	0.66
Threshold	0->1	PI: 9	0.26	0.03	9.82	0	0.26

Table C.5 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Threshold	0->1	PI: 10	0.18	0.03	7.15	0	0.18
Threshold	0->1	PI: 19	0.6	0.03	21.87	0	0.6
Threshold	0->1	PI: 27	-0.06	0.03	-2.15	0.03	-0.06
Threshold	0->1	PI: 36	0.63	0.03	22.6	0	0.63
Threshold	0->1	PI: 44	0.56	0.03	20.51	0	0.56
Threshold	0->1	PI: 45	0.4	0.03	15.04	0	0.4
Threshold	0->1	PI: 48	1.37	0.04	37.22	0	1.37
Threshold	0->1	PI: 53	0.37	0.03	14.06	0	0.37
Threshold	0->1	PI: 59	1.03	0.03	32.85	0	1.03
Threshold	0->1	PI: 60	0.39	0.03	14.72	0	0.39
Threshold	0->1	PI: 63	0.16	0.03	6.24	0	0.16
Threshold	0->1	PI: 65	0.57	0.03	21.02	0	0.57
Residual		SMFQ: 1	0.42	0	181.73	0	0.42
Residual		SMFQ: 2	0.54	0	288.92	0	0.54
Residual		SMFQ: 3	0.73	0	643.16	0	0.73
Residual		SMFQ: 4	0.78	0	622.03	0	0.78
Residual		SMFQ: 5	0.26	0	472.51	0	0.26
Residual		SMFQ: 6	0.61	0	489.21	0	0.61
Residual		SMFQ: 7	0.49	0	549.35	0	0.49
Residual		SMFQ: 8	0.24	0	383.67	0	0.24
Residual		SMFQ: 9	0.47	0	351.1	0	0.47
Residual		SMFQ: 10	0.42	0	361.32	0	0.42
Residual		SMFQ: 11	0.3	0	213.57	0	0.3
Residual		SMFQ: 12	0.39	0	427.06	0	0.39
Residual		SMFQ: 13	0.33	0	223.16	0	0.33
Residual		AEB: 1	0.81	0	456.76	0	0.81
Residual		AEB: 3	0.49	0	127.83	0	0.49
Residual		AEB: 4	0.67	0	340.06	0	0.67
Residual		AEB: 12	0.4	0.01	69.93	0	0.4
Residual		AEB: 13	0.46	0	221.19	0	0.46
Residual		AEB: 21	0.65	0	233.66	0	0.65
Residual		AEB: 22	0.61	0	218.44	0	0.61
Residual		AEB: 28	0.52	0	203.18	0	0.52
Residual		AEB: 30	0.4	0	102.12	0	0.4
Residual		AEB: 31	0.65	0	244.68	0	0.65
Residual		AEB: 37	0.54	0.01	98.81	0	0.54
Residual		AEB: 39	0.6	0	128.78	0	0.6

Table C.5 – continued from previous page

Parameter type	Factor or threshold	Item or factor	Unstd. estimate	Standard error	Z-score	P-value	Std. estimate
Residual		AEB: 40	0.39	0	83.55	0	0.39
Residual		AEB: 47	0.46	0	128.31	0	0.46
Residual		AEB: 55	0.48	0	111.69	0	0.48
Residual		AEB: 56	0.67	0	277.31	0	0.67
Residual		AEB: 61	0.53	0	212.56	0	0.53
Residual		AEB: 64	0.48	0	194.75	0	0.48
Residual		PI: 9	0.37	0	188.74	0	0.37
Residual		PI: 10	0.53	0.01	65.28	0	0.53
Residual		PI: 19	0.5	0	202.27	0	0.5
Residual		PI: 27	0.52	0	230.63	0	0.52
Residual		PI: 36	0.38	0	88.91	0	0.38
Residual		PI: 44	0.49	0	115.61	0	0.49
Residual		PI: 45	0.41	0.01	61.73	0	0.41
Residual		PI: 48	0.44	0.01	61.13	0	0.44
Residual		PI: 53	0.31	0	100.09	0	0.31
Residual		PI: 59	0.29	0	77.66	0	0.29
Residual		PI: 60	0.4	0	170.53	0	0.4
Residual		PI: 63	0.13	0.01	20.83	0	0.13
Residual		PI: 65	0.53	0	208.41	0	0.53
Variance		General Factor	0.21	0.02	9.88	0	1
Variance		SF1	0.37	0.03	14.47	0	1
Variance		SF2	0.09	0.02	4.67	0	1
Variance		SF3	0.06	0.02	3.39	0	1

Table C.5: Parameter estimates from bifactor model fit to combined SMFQ and BSSI items with a robust weighted-least-squares (WLSMV) estimator to 25 imputed data sets in NSPN. GF = general factor. SF1 = specific SMFQ factor. SF2 = specific AEB factor. SF3 = specific AEB factor. Unstd. estimate = unstandardised estimate. Std. estimate = standardised estimate.

This model fit the data from 25 imputed datasets excellently with a WLSMV estimator (CFI = 0.975, TLI = 0.971, RMSEA = 0.039). There were no negative residual item variances. Table C.5 shows full parameter estimates.

The general distress factor explains the majority of the variance in psychosis and distress items

I calculated ω statistics from the a full-information MLR-estimated bifactor model with the negative loading on the specific PI factor removed. Again, the fit fell just short of predefined criteria for CFI and TLI, though RMSEA indicated very good fit (CFI = 0.895, TLI = 0.884, RMSEA = 0.035).

Figure C.3 Information distributions of self-report PEs and depressive symptoms in ROOTS

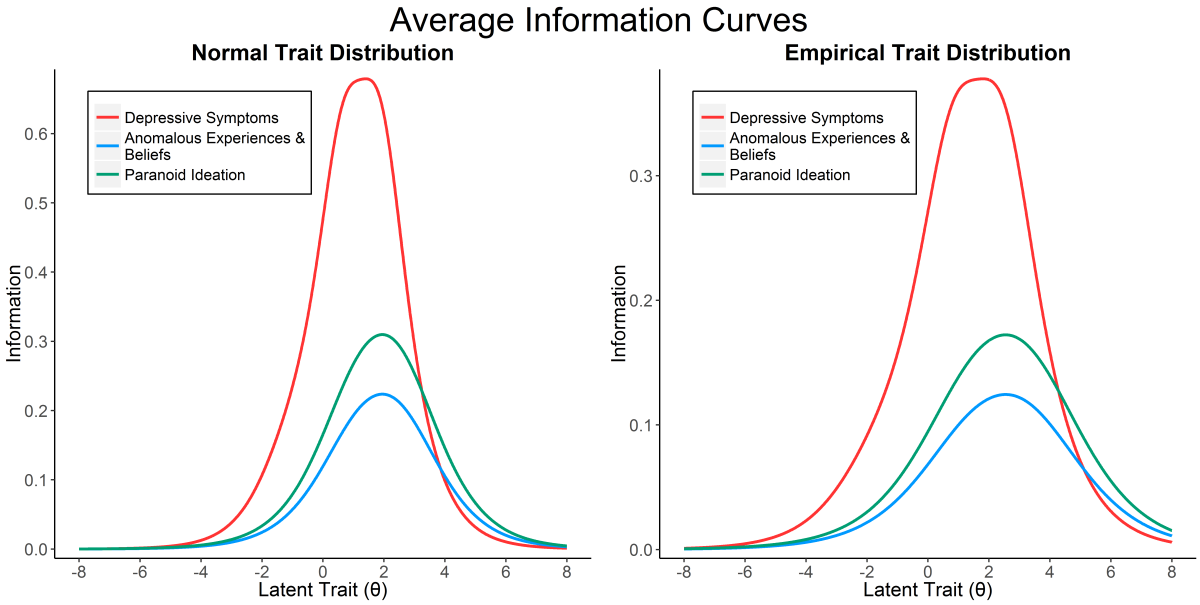

Figure C.3: Information distributions were estimated using parametric item response theory analyses with two-parameter logistic curves in NSPN. The curves quantify where along the distribution of a latent trait an item contributes information and thus is able to measure common mental distress. Anomalous Experiences & Beliefs and Paranoid Ideation both measured a slightly more severe range of distress than depressive symptoms. The distributions were very similar for both traits assumed to have a normal distribution and empirically-estimated distributions.

The general factor explained 67.5% of the item variance. The specific factor of SMFQ items explained 8.5% of the variance, the specific factor of AEB_{SPQ} items explained 21.1% of the variance and the specific factor of PI items explained 1.9% of the variance. 1.0% of the item variance was residual error.

Anomalous experiences and beliefs measure more severe common mental distress than paranoia and traditional depressive/anxious and anxious symptoms

SMFQ, AEB_{SPQ} and PI_{SPQ} items measured similar severity ranges of mental distress, shown by mostly overlapping information distributions for both the Gaussian and the empirical latent trait distribution (Figure C.3). AEB_{SPQ} and PI_{SPQ} items both measured a more severe range of mental distress, indicated by these items uniquely contributing information to the higher end of the distress trait. PI_{SPQ} items measured a slightly more severe range than AEB_{SPQ}, in contrast to the results in ROOTS.

SMFQ items contributed more information to the distress factor, on average, than AEB_{SPQ} items, indicated by higher AUC for the information distributions of SMFQ items than AEB_{SPQ} items and PI_{SPQ} items, indicated by Wilcoxon rank-sum test (SMFQ: mean AUC = 2.62, SD = 0.72, AEB_{SPQ}: mean AUC = 1.00, SD = 0.20, W = 233, $p < 0.0001$; PI: mean AUC = 1.54, SD = 0.30, W = 151, p = 0.0003). PI_{SPQ} items also contributed more information to the distress factor than AEB_{SPQ} items (W = 15, $p < 0.0001$).

Variance in sum scores attributable to general distress and specific factors

See Table C.6 for full results of linear regressions on sum scores.

44.4% of the variance in AEB scores was explained by the general distress factor, while the specific factors of SMFQ and PI items explained negligible amounts and the specific factor of AEB items explained 58.0%. Together, the distress factor and the specific AEB factor explained 91.5% of the variance.

87.6% of the variance in PI was explained by the general distress factor. The specific factors of SMFQ and AEB each explained negligible variance and the specific factor of PI items explained only 10.4%. This suggests that paranoia always tends to manifest in conjunction with distress. All factors together explained 94.2% of PI

Table C.6: Proportion of variance in sum-scores on self-report PEs and depressive symptoms that is explained by the general and specific factors from the bifactor model in NSPN.

Factor	AEB_{SPQ}	PI_{SPQ}	SMFQ
GF	0.44	0.88	0.45
SF1 (SMFQ)	0	0	0.65
SF2 (AEB)	0.58	0	0
SF3 (PI)	0	0.1	0
GF + SF1 (SMFQ)	0.46	0.89	0.94
GF + SF2 (AEB)	0.91	0.89	0.46
GF + SF3 (PI)	0.46	0.93	0.47
All factors	0.92	0.94	0.94

Table C.6: AEB = Anomalous Experiences & Beliefs, PI = Paranoid Ideation, SMFQ = Short Mood and Feelings Questionnaire. SPQ = Schizotypal Personality Questionnaire.

These results replicate findings using interview-assessed PEs (Stochl et al., 2015) and, in the ROOTS cohort, shows that this continuum is true of symptoms measured over the same recent two-week interval. This supports PEs as a transdiagnostic manifestation of psychopathology in the general population and suggest convergent validity of self-report and interview-verified PEs. This is important as self-report instruments are easier and cheaper to administer and might enable far larger sample sizes or repeat measurements than would be feasible with interview assessments. This study has the strengths of utilising data from two general population cohorts and replication of results in independent cohorts. The study is limited by inability to generalise these results to other instruments and by relatively simplistic interpretation of complex latent variables.

C.5 References

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Appendix D

Study documents for Chapter 12

UNIVERSITY OF CAMBRIDGE

Department of Psychiatry
William Hardy Building
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Downing Street
Cambridge, CB2 3EB

Version1 (12/02/13)

Participant Number:

CONSENT FORM (Psychophysical Testing)

Ethics Approval Ref: PRE.2013.31
Title of Study: Psychophysical and fMRI Investigation of Feed-Back Processes in the Human Visual System

Chief Investigator: Prof. Paul Fletcher

Having read the Information Sheet (12/02/13 Version1 – psychophysical testing), please read the following statements and initial to show that you have understood and agree to the conditions. Please do not hesitate to ask, should you have any further questions.

1. I confirm that I have read, understood, and accept the conditions contained in the information sheet, version1 – psychophysical testing dated 12/02/13, for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without any penalty. ☐

3. I understand that I will be asked to complete some questionnaires designed to evaluate my everyday experiences and beliefs. I also understand that there is no obligation to answer these questions. ☐

4. I understand that the data will be accessed by the research team and by collaborating researchers or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to these records. ☐

5. I understand that I will be paid £8 per hour for participating in this study. ☐

6. I agree to take part in the above study. ☐

……. ……. ……...
Name of Participant Date Signature

……. ……. ……..
Name of Research Team Member Date Signature

If you have any further questions or worries please contact;

Either:

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Tel: 01223 768501
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Prof. Paul Fletcher (chief investigator)
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Cambridge, CB2 2QQ

UNIVERSITY OF CAMBRIDGE

Dept. of Psychiatry

PARTICIPANT INFORMATION SHEET –

Psychophysical Testing

Version 2
Date: 19/03/2013

Study title: Psychophysical and fMRI Investigation of Feed-Back Processes in the Human Visual System

The project has received ethical approval from the Psychology Research Ethics Committee of the University of Cambridge.

We would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully and talk to others about the study if you wish.

Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Part 1.

What is the purpose of this study?
The purpose of this study is to investigate how the visual system processes images.

Why have I been invited?
The aim of the present study is to better understand the computational processes mediating visual perception by healthy participants.

Do I have to take part?
It is up to you to decide. We will describe the study and go through this information sheet. We will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason.

What will happen to me if I take part?
The study will involve a minimum of one and a maximum of ~~or several test~~ five test sessions depending on which specific experiment you take part in.~~,~~ E~~e~~ach session will last~~ing~~ at most 90 minutes. In case you take part in more than one test session, the sessions will be separated by a minimum of two days. During the testing session you will be shown neutral images and you will be asked to make simple decisions using a computer keyboard. After completion of the experiment, you will be asked to complete some questionnaires designed to evaluate your everyday experiences and beliefs. Some of the questions will be about unusual experiences/beliefs while others are about typical experiences/beliefs. You are under no obligation to answer these questions.

You will be paid £8 per hour for your participation, which you will receive at the end of final session you take part in.

What about time and travel expenses?

You will be paid £8 per hour for your participation, which you will receive at the end of final session you take part in.

What are the possible benefits of taking part?
While we hope that, should you choose to participate in the study, you would find it interesting and comfortable, there are no direct benefits to you of taking part. You will, however, be compensated for time and inconvenience. We will pay you £8 per hour for your participation.

What if there is a problem?
Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Please contact either Dr Christoph Teufel or Prof. Paul Fletcher (see contact details at the end of this information sheet).

Will my taking part in the study be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Part 2.

Will my taking part in the study be kept confidential?
The data derived from this study will be stored on a secure network and on password protected computers. Only authorised members of the Behavioural and Clinical Neuroscience Institute (BCNI) and members of the research group will have access to the data. The University is deemed to be the Data Controller and all enquiries concerning access to the data should be addressed to him. The Administrator of the BCNI will be able to tell you the name and address of this officer.

What will happen to the results of the research study?
When data from several volunteers is collected, it will be analyzed and written up for publication in a scientific journal. The results may also be presented at scientific meetings, or in talks at academic institutions. Results will always be presented in such a way that data from individual volunteers cannot be identified. Data will be kept securely for a minimum of 10 years and possibly indefinitely in the BCNI data archive in accordance with good research practice.

Who is organizing and funding the research?
This study is organized by a research team headed by Prof. Paul Fletcher at the University of Cambridge, Department of Psychiatry, Brain Mapping Unit. The research is funded by a grant awarded to Prof. Paul Fletcher by the Wellcome Trust.

Are there compensation arrangements if something goes wrong?
The University of Cambridge has approved this study and arranged insurance cover in the unlikely event of something going wrong.

You are entirely free to withdraw from the study at any time without having to explain why. Non-participation would not affect your future treatment in any way.

If you have any questions about the study (or if you wish to complain), please contact:

Name: Prof. Paul Fletcher
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Department of Psychiatry, Brain Mapping Unit

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